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THE RÔLE OF THE AUTONOMOUS MOVEMENTS OF THE GASTROINTESTINAL MUCOUS MEMBRANE IN DIGESTION*

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THE discovery that the mucous membrane, through its power of autonomous movement, is able to take an active part in the formation of the inner relief of the digestive canal, makes it probable that the movements of the mucous membrane have an independent function in the mechanical regulation of digestion.

More detailed knowledge of the rôle played by the movements of the mucous membrane in the mechanical regulation of digestion could, however, not be obtained before it had been settled whether the contents of the digestive canal take such a position in regard to the mucous membrane relief that we are entitled to suppose that their distribution is brought about by coordinated movements of the mucous membrane.

I attempted to attain this aim by utilizing the experience that the mucous membrane relief maintains its natural shape when it is fixed by injecting formalin into the vascular system shortly after death. After feeding animals with a chosen diet and killing them during the course of digestion, then by fixation in the manner mentioned, there can be obtained a lasting picture of the distribution of the ingesta in regard to the mucous membrane relief. In man also the arrangement of the mucous membrane relief in relation to the ingesta has been studied in a series of cases, where the cadavers had been treated in the manner mentioned above a few hours after death.

The results of my investigations on the functional task of the mucous membrane movements, published in previous papers, *inter alia* as the Rieder Lecture 1934,** *may be summarized as follows:*

The folds of the mucous membrane adapt themselves continually to the degree of contraction of the muscle wall, but at the same time the mucous membrane relief adapts itself to the consistency and form of the contents of the digestive canal and to the regulation of the forward passage of these.

With maximal contraction of the muscle wall and with an empty lumen, the mucous membrane fills out the muscle tube and forms an "initial relief" with an appearance which is specific for each particular segment of the digestive tract. In places where the digestive canal is very distended the mucous membrane adopts a uniform "final relief." In the stomach, colon and rectum, except the sphincters, the mucous membrane folds then disappear, while in the small intestine transverse folds persist even in the state of marked distention.

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* Presented at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

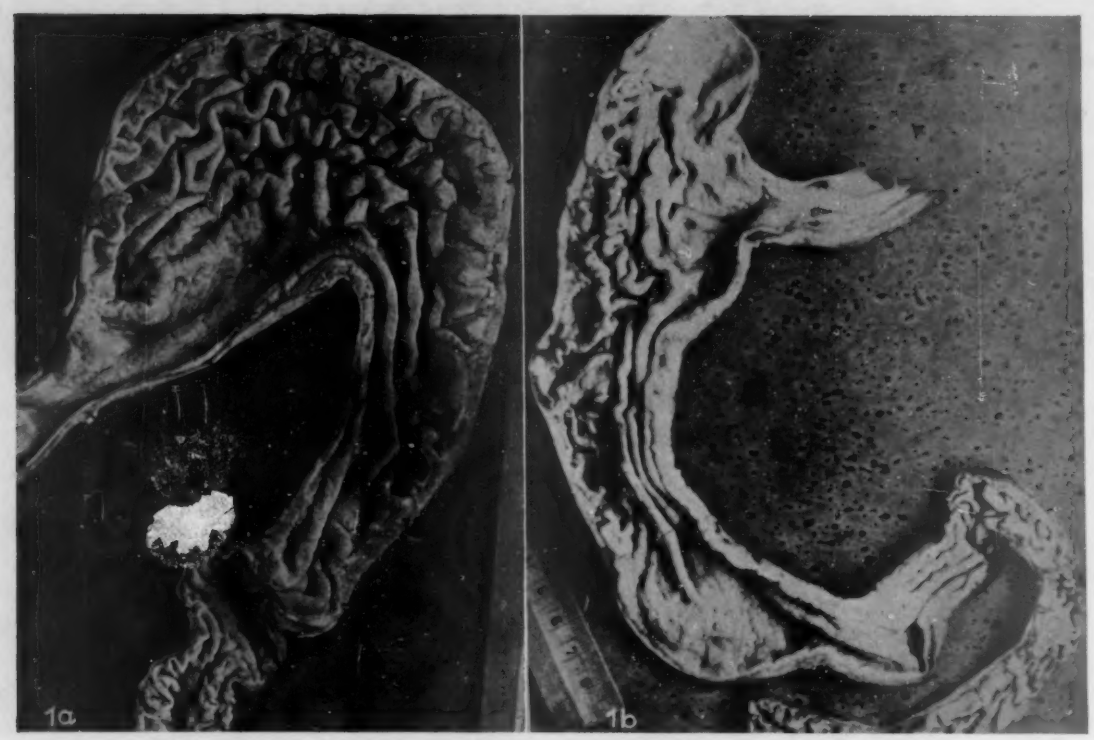

FIG. 1. *a*, initial relief of a human stomach; *b*, beginning transformation of the initial relief to a working relief in a human stomach.

A certain contraction of the muscular tube is necessary for the formation of macroscopic folds in the mucous membrane. After such a contraction the mucous membrane, by alternately producing a smooth surface or folds of various sizes and forms, without altering the diameter of the muscular tube, is able to form a "working relief," the shape of which can vary greatly at the same site.

In the small intestine, where the contents are fluid, the form of the relief is the only guidance for conclusions as to the function of the mucous membrane movements. In the stomach, colon and rectum, which may contain fluid as well as solid and gaseous substances, a mucous membrane relief is formed which is characteristic for the consistency and form of the contents. When the contents are fluid or semifluid, the mucous membrane relief usually shows a more uniform and regular arrangement, often conserving at the same time at a certain extent the general type of the "initial relief." The soft contents are then divided by projecting folds and in this way dispersed among "digestive chambers" of various sizes. When the contents are solid or a mixture of solid and semisolid, the mucous membrane encloses the solid particles with which it comes in contact in cup-like chambers. Even with marked contraction of the muscle wall, the initial relief alters considerably with such contents. At the site of local contraction of the muscle wall, which frequently occurs between portions of contents of different consistency, the mucous membrane can assume forms which narrow the lumen more or less, or it can adopt a low relief which leaves the lumen free in spite of a marked contraction of the muscle wall. Everywhere in the digestive canal where gas accumulates the mucous membrane seems to form cavities with smooth surfaces and regular contours.

There thus exist two coordinated but independent mechanisms of movement in the digestive canal. The musclar tube and its anatomically preformed sphincters dis-

tribute the contents of the intestinal canal into a number of large containers in preparation for the various main processes of digestion. They also have the task of transporting these contents in large portions.

The mucous membrane transfers the force from the muscle wall power station to the countless special apparatus, which in turn are formed by the mechanical workshop of the mucous membrane. This workshop also provides the power for the individual mechanical processes of the work of digestion.

The mucous membrane movement mechanism is of such a construction that it can build work machines of various forms and sizes at the same site and out of the same material; for instance, cisterns for biochemical work or apparatus for filtration, sorting and transportation, all according to the digestive requirements of the moment.

On this occasion I shall show *a series of pictures of my anatomical preparations which illustrate a number of the functional variations of the mucous membrane relief.*

EMPTY STOMACHS AND STOMACHS WITH FLUID OR SEMIFLUID CONTENTS

Figure 1*a* shows the mucous membrane relief on the posterior surface of an almost entirely empty, greatly contracted human stomach. It presents the initial or resting relief known from roentgenograms of a contracted stomach. The muscle sac is filled with high, closely compressed mucous membrane folds. Fissure-shaped furrows between smooth longitudinal folds form in the well-known manner along the lesser curvature a connecting link (in this case closed) between the upper part of the stomach and the pylorus. For the rest the initial relief constitutes a bed of anastomosing folds which stands ready to receive and distribute, in a way to be described below, the food which enters the stomach.

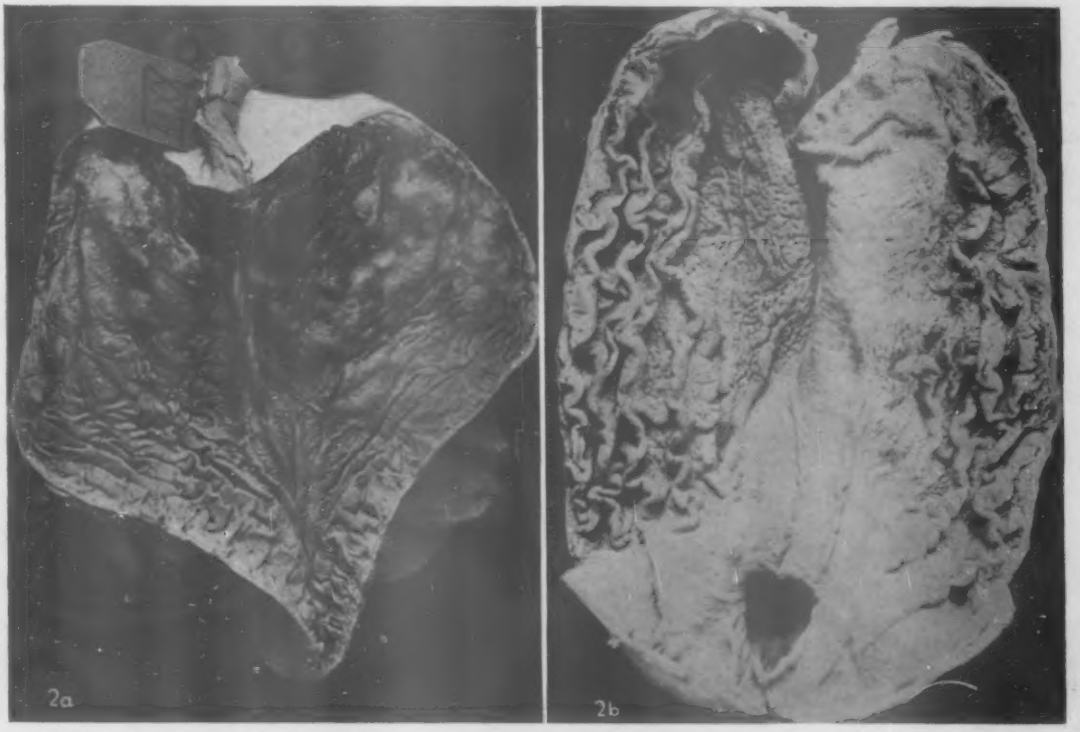

Fig. 2. *a*, working relief in a human stomach. The upper half of the stomach forms a wide, smooth walled reservoir; the lower half shut off by high folds. *b*, working relief in a human stomach. Cylindrical receptacle on the lesser curvature. A system of digestive chambers on the greater curvature. A circular muscle-mucous-membrane fold at the entrance to the evacuation canal.

Figure 1*b* shows an incipient transformation of the initial relief into a working relief in a human stomach. At three places, namely in the fornix, in the corpus close to the cardia, and at the angulus, the folds of the high relief have transformed themselves into low relief, so that in the bed of folds there have formed small receptacles, which enclosed thin fluid contents and air. Here and there within the bed of folds in the greater curvature the folds have separated from each other to form irregular, small digestive chambers with semifluid contents. In the lesser curvature and the canalis the initial relief remains in about its original shape and closes the lumen by its high, firmly compressed folds.

Figure 2*a* shows a human stomach, where the fornix (=the vault of the stomach above the cardia) and the upper half of the corpus have distended themselves into a wide, smooth-walled reservoir, which enclosed fluid contents and air. The lower half of the stomach is cylindrically contracted and shut off from this wider reservoir by high folds engaging closely with each other like interlaced fingers.

Fig. 3. Transverse sections of a pig stomach. Working relief.

The human stomach whose mucous

membrane relief is shown in Figure 2*b* also contained semifluid chyme and air. Here there has been formed a broad, cylindrical reservoir close to the lesser curvature within the corpus and in the sinus (=the pocket-formed junction between the corpus and the evacuation canal, the "canalis egestorius"). Within this reservoir there is a low relief of varying type. At the greater curvature there remains in the fornix and the corpus a high relief, forming a system of irregular digestive chambers. A circular muscle-mucous-membrane fold surrounds the entrance to the "canalis egestorius."

Figures 3 and 4 show a series of transverse sections from two pig stomachs.

In both cases, the upper part of the stomach (fornix+corpus) (sections *A–E*, Fig. 3, and sections *J–N*, Fig. 4) formed a rather broad reservoir, where the greater part of the contents had accumulated. By means of high mucous membrane folds this reservoir is divided into digestive chambers of different sizes, which were filled with porridge-like contents. The lower part of the stomach (sinus and canalis) (sections *F–H*, Fig. 3, and *O–Q*, Fig. 4) is in both instances cylindrically contracted and presents a mucous membrane relief which varies greatly in appearance, both on adjacent parts of the same stomach and on analogous areas within the two stomachs.

Within the one stomach (Fig. 3) the lumen in the lowermost part of the corpus and in the transverse stomach forms an open tube, flattened at the sides and divided by means of a few simple, band-like, longitudinal folds (section *F–H*), which extend the whole way to the pylorus.

In front of the pylorus in pig stomachs there is in the lesser curvature a constant, broad, sponge-shaped barring formation in the mucous membrane (the "torus pyloricus"). Two longitudinal folds which extend downwards to the pylorus (in section *H*) rest their free edges against this, thus forming three narrow evacuation or filtering tubes in front of the pylorus.

In the other pig stomach (Fig. 4) the lowest part of the great reservoir (section

Fig. 4. Transverse sections of a pig stomach. Working relief in all parts of the stomach differing from those in Figure 3.

N) is, in spite of the width of the muscular tube, almost entirely closed by a mucous membrane formation of just the same construction as the mucous membrane bar in the human stomach which has just been demonstrated (Fig. 2*a*).

The space between the flat surfaces of the muscular wall is filled by high mucous membrane folds, interlacing with each other and filling the furrows on the opposite side. Only close to the lesser curvature there is left open a cylindrical evacuation passage, where there are low, longitudinal folds so close to each other that their ridges form together a lumen with an almost smooth wall. At the entrance of the sinus (section *O*), most of the folds have flattened out so that a broad, flat passage opens there.

Within the canalis (Fig. 4, *P*) lamellar-shaped longitudinal folds suddenly make their appearance again, but here they embrace each other only incompletely and so

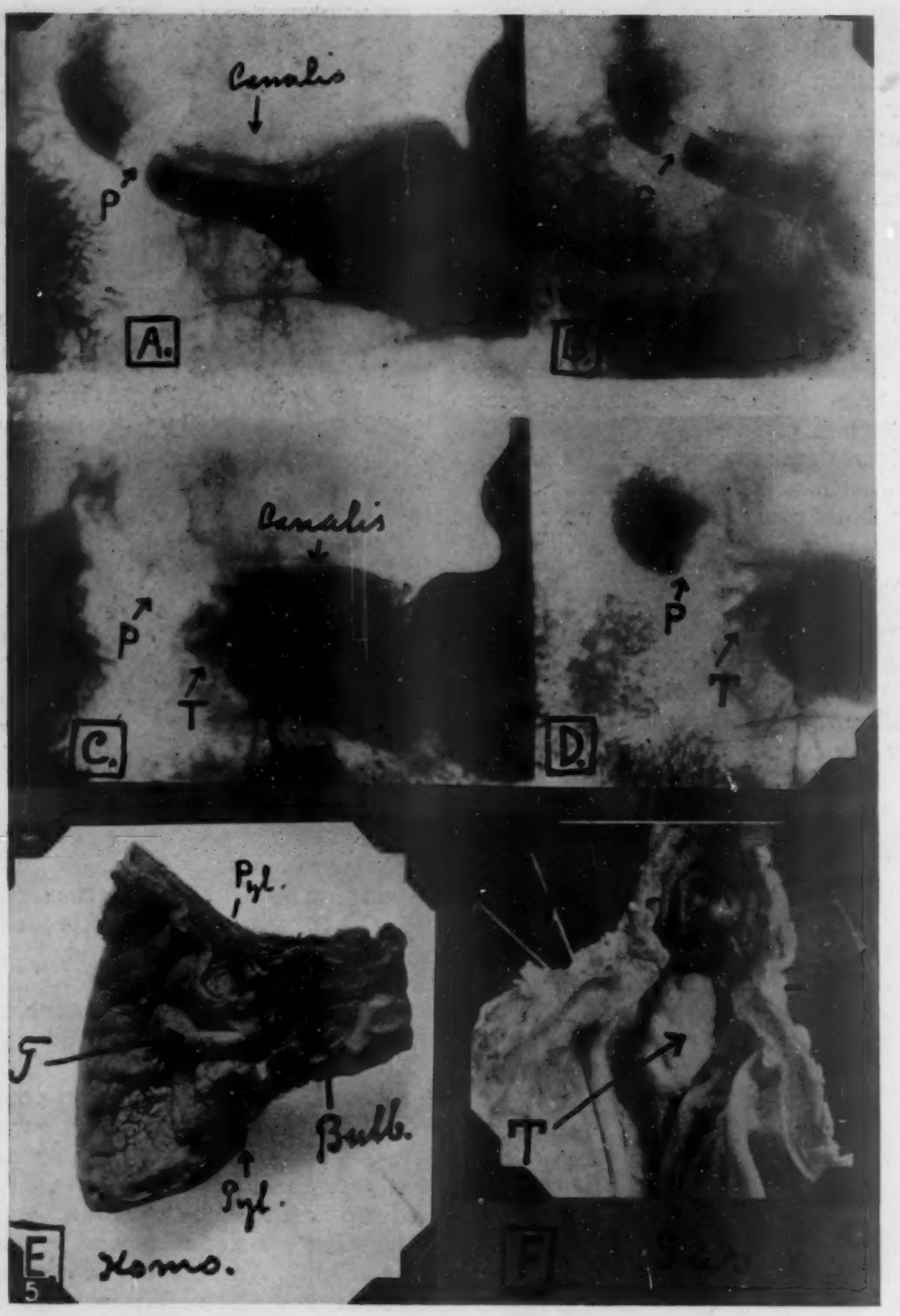

FIG. 5. *A–D*, roentgenograms of various relief formations regulating the passage of a fluid meal through the evacuation canal of a human stomach. *T* = prepyloric mucous membrane bar. *P* = pylorus. *E*, functional prepyloric bar (*T*) in a human stomach. Resection specimen. *F*, anatomical preformed prepyloric mucous membrane bar (*T*) in a pig stomach.

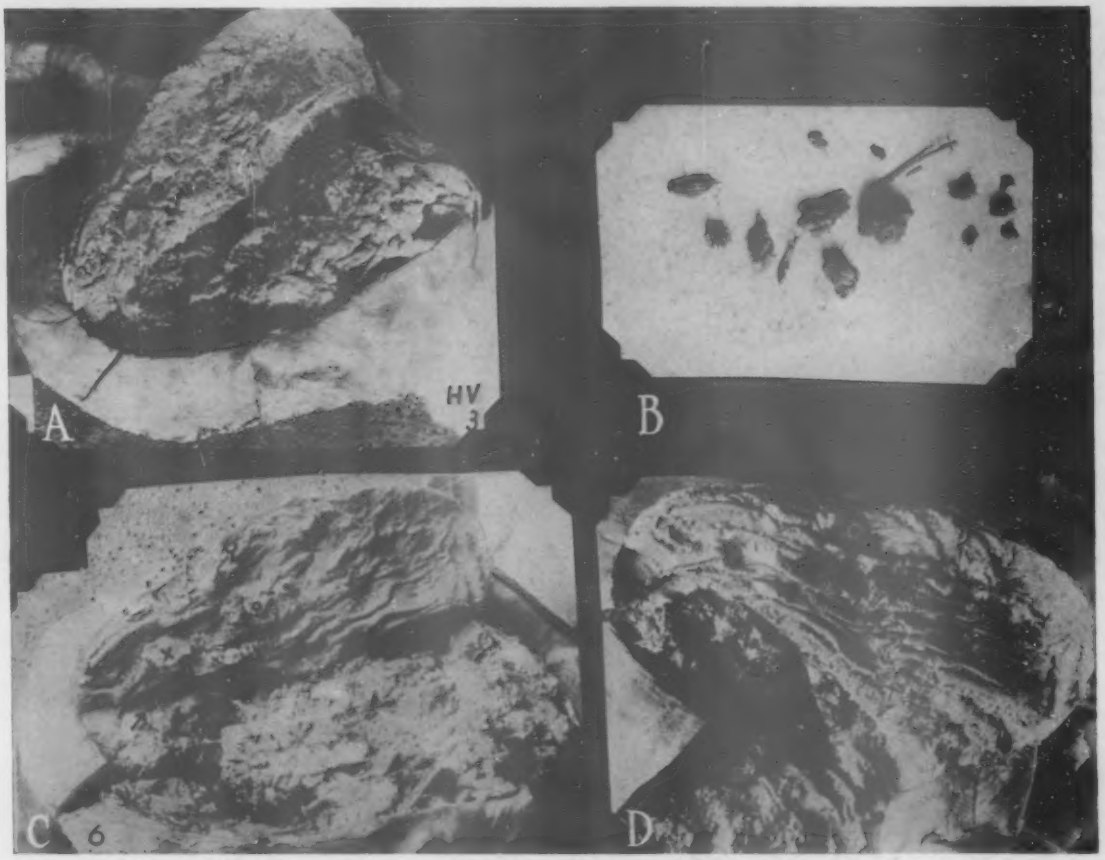

Fig. 6. A patch of the left side of a dog's stomach. *A*, mucous membrane surface covered with a film of coagulated chyme; *C*, chymous film brushed off. Gastric contents enclosed in mucous membrane chambers; *B*, contents removed from the chambers; *D*, empty digestive chambers.

give rise to a system of fissure-shaped canals confluent in the middle of the lumen, thus forming a filtering apparatus. Immediately in front of the pylorus, the longitudinal folds sink down and arrange themselves so closely to each other and to the pylorus bar that their edges together constitute an almost smooth wall (section 2).

In this way, the mucous membrane relief in the canalis converts itself in front of the pylorus into one single narrow evacuation duct at the same site where in the former example (Fig. 3, *H*) it divided the lumen into three tubes of about equal width. The contents of the system of passages in front of the pylorus were considerably more fluid than in the large reservoir in the upper part of the stomach, while in the duodenal bulb the consistency was that of thin homogeneous gruel.

Figures 3 and 4 give a good idea of the capacity of the mucous membrane to vary the width and the form of the lumen by the formation of different reliefs within the same area of the stomach and in this way to act on the distribution and passage of the contents.

Figures 5 *A*, *B*, *C* and *D* are roentgenograms of a human stomach taken in prone position at intervals of about one-half minute. They show various stages of the passage regulation during digestion of a fluid contrast meal. At the same place there appear here one after another mucous membrane formations resembling those just demonstrated in the anatomical preparations of the pig stomachs. In Figures 5 *A* and *B*, the contents are strained off through the evacuation canal within smooth longitudinal mucous membrane

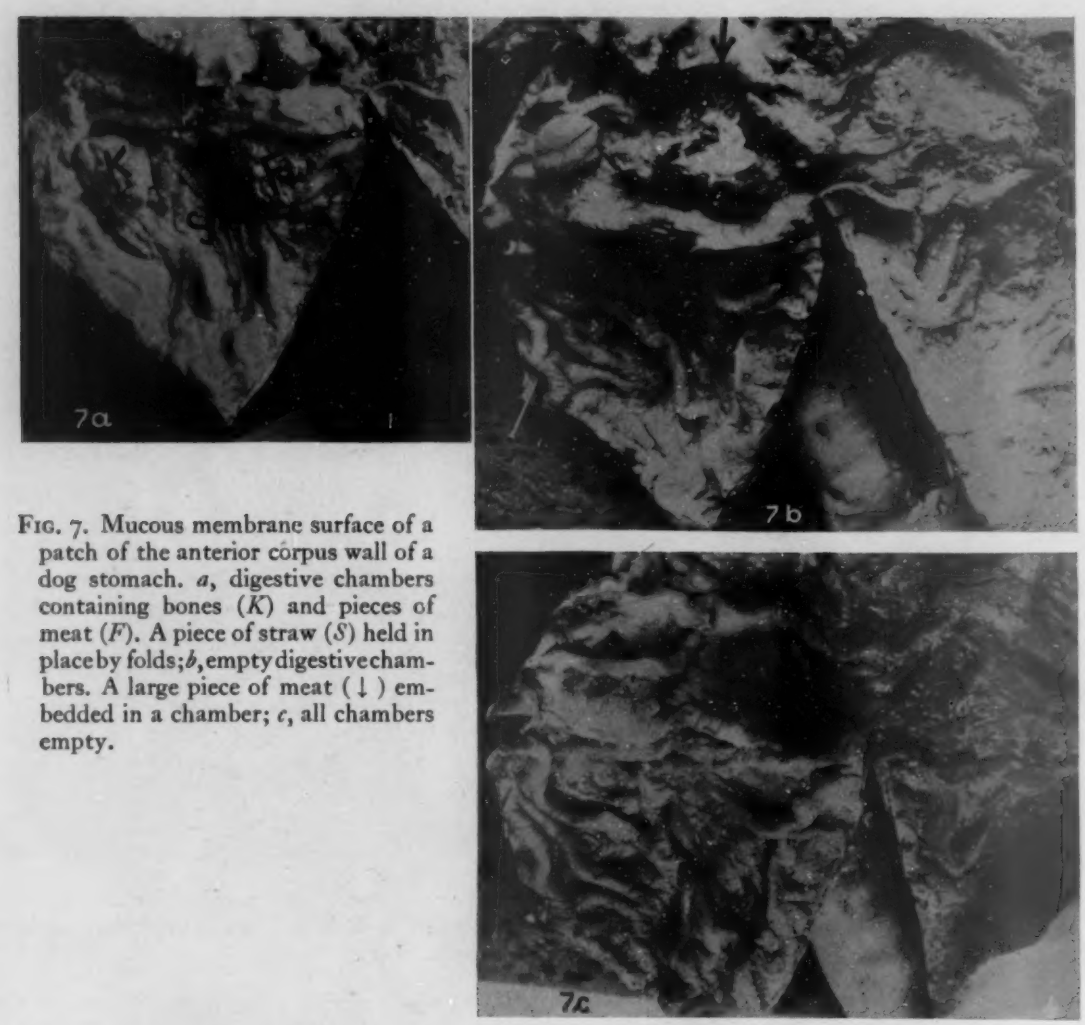

Fig. 7. Mucous membrane surface of a patch of the anterior corpus wall of a dog stomach. *a*, digestive chambers containing bones (*K*) and pieces of meat (*F*). A piece of straw (*S*) held in place by folds; *b*, empty digestive chambers. A large piece of meat (↓) embedded in a chamber; *c*, all chambers empty.

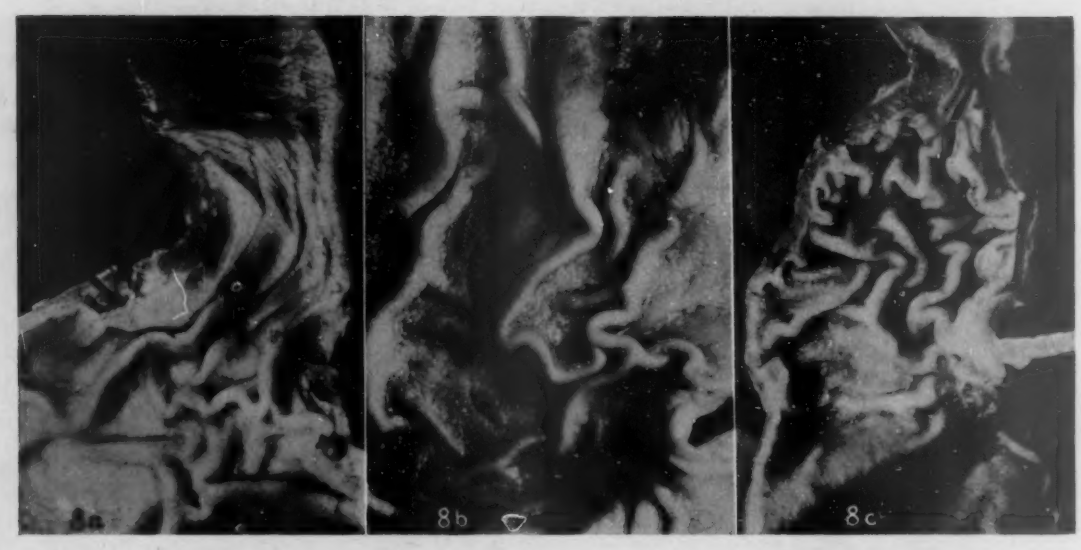

Fig. 8. Digestive chambers in the stomach of a cat after it had eaten two mice.

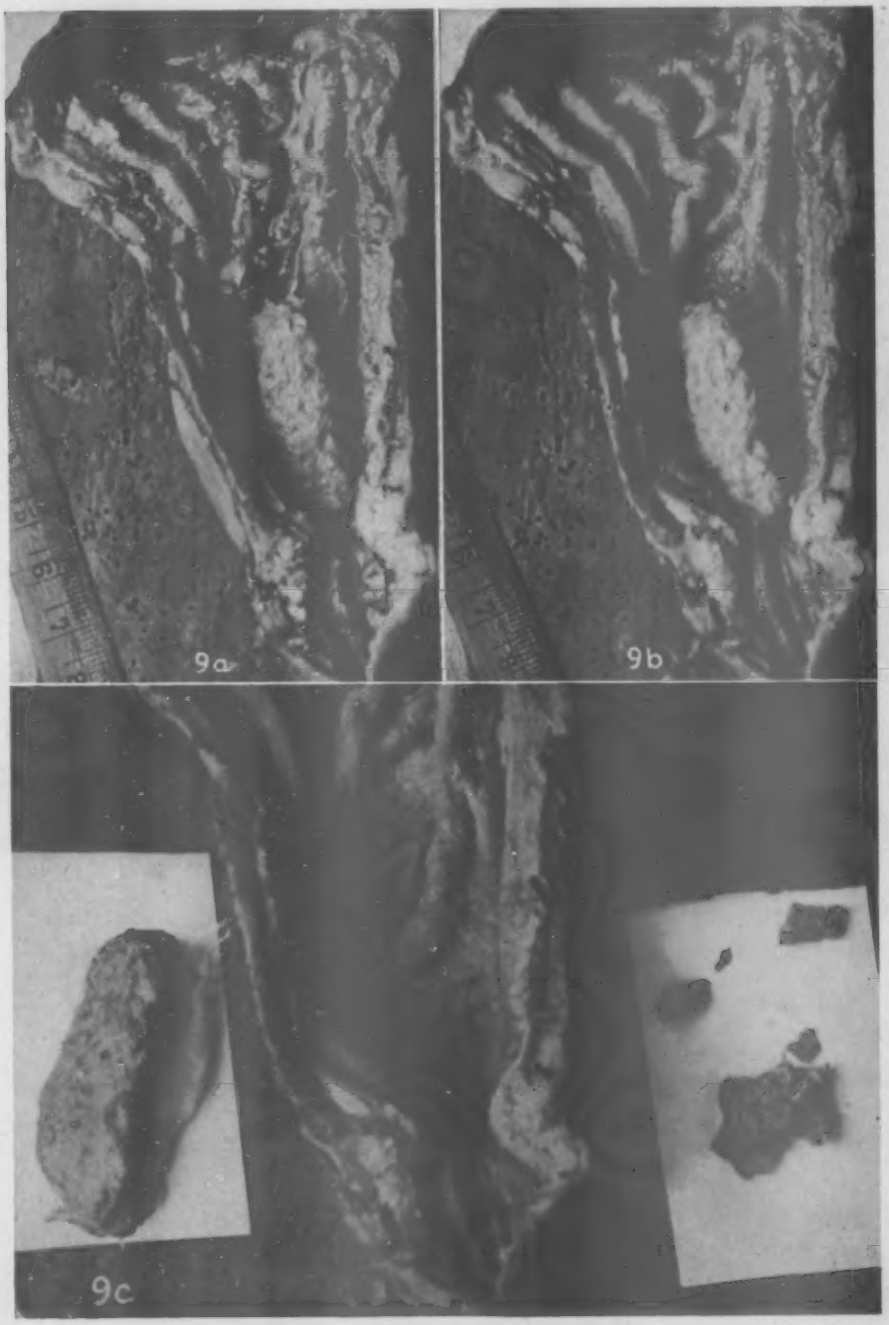

Fig. 9. *a*, several pieces of meat embedded in corresponding chambers of a human stomach; *b*, mucous membrane cleaned; *c*, a few pieces of meat removed from the now empty chambers.

fissures. In Figures 5*C* and *D* the passage of the contents is barred by a mucous membrane formation composed of a close network of folds in front of the pylorus.

Figure 5*E* shows the anterior wall of a resection preparation from the pyloric area of a human stomach fixed in formalin shortly after the operation. We see here a cushion of mucous membrane folds (*T*), the torus pyloricus, which bars the entrance into the pylorus and corresponds to the functional pylorus bar visible in the roent-

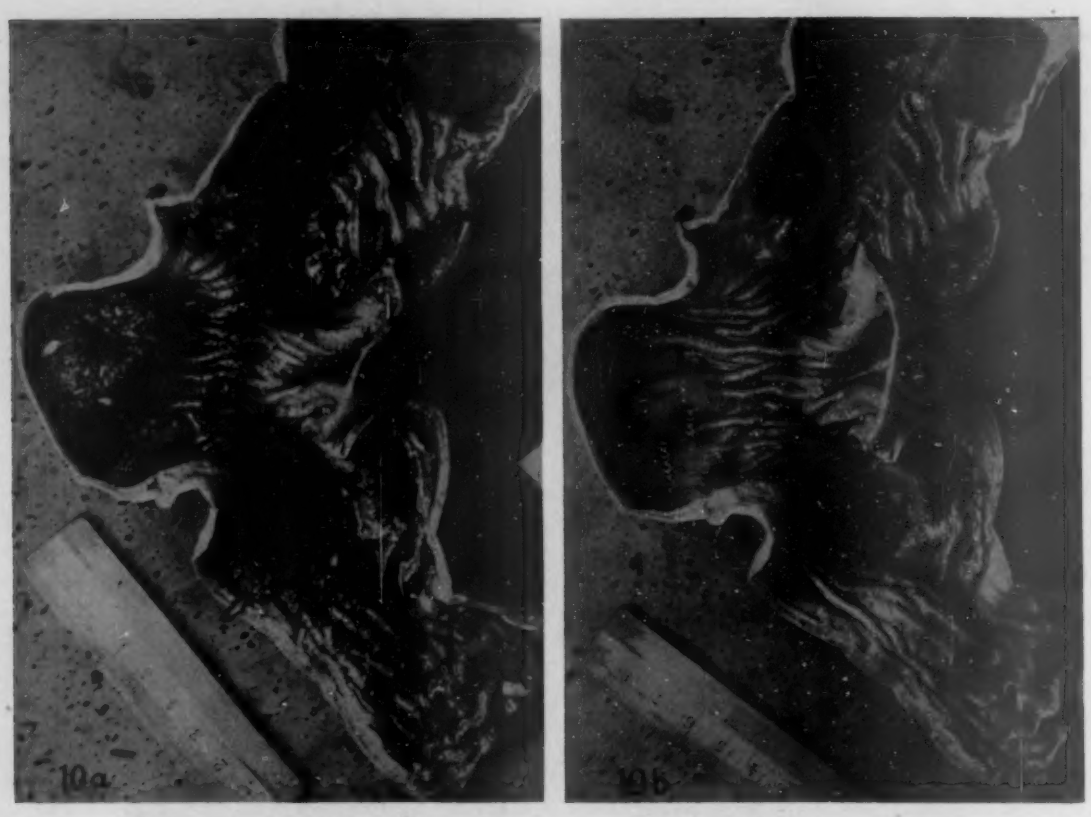

FIG. 10. Work relief of a loop of the small intestine of a horse. Haustra-like digestive chambers. *a*, contents *in situ*; *b*, mucous membrane relief, freed from contents.

genogram of the living human stomach. Figure 5*F* reminds us of the fact that in the pig stomach and in the abomasum of ruminants such a barring structure is a constantly present anatomical formation.

STOMACHS CONTAINING SOLID FOOD AND FOOD OF VARYING CONSISTENCY

Figures 6*A*, *C* and *D* show a part of the left side of a dog stomach where a flap of the wall of the corpus nearest the lesser curvature has been turned up. An hour and a half before death the dog had had a meal of meat, bone and cartilage. In Figures 6 *A* and *C* one sees through the opening the firmly compressed contents in the corpus. In Figure 6*A* the surface of the mucous membrane of the flap is covered by a film of chyme which has been coagulated by the formalin.

In Figure 6*C* this film has been delicately brushed away. One can see that numerous small bits of bone and cartilage together with a couple of little pieces of straw have sunk into the surface of the mucous membrane. When these pieces (Fig. 6*B*) have been removed, we find that they were enclosed in small chambers like a tooth in its alveolus (Fig. 6*D*).

Figures 7*a*, *b* and *c* show an anatomical preparation obtained in a similar way. We see a flap of mucous membrane from the greater curvature on the lower part of the corpus of a dog which had also been fed with meat, bone and cartilage. This shows how the whole of the mucous membrane is divided into chambers where the pieces of bone, cartilage and meat lie sunk between walls of mucous membrane. In one place there is visible a piece of straw surrounded by folds of mucous membrane.

Figures 8*a*, *b* and *c* show the mucous membrane relief of the stomach of a cat which had consumed two mice. The cardia (Fig. 8*a*) is closed by longitudinal folds which descend from the esophagus and are

connected by a graceful ring of mucous membrane arcades. Below this there is visible a series of shallow mucous membrane chambers. Deep digestive chambers are seen on the greater curvature in the corpus (Fig. 8*b*). The sinus, which contained a compressed, soft mass of meat, has smooth walls, while the mucous membrane relief in the canalis forms numerous small chambers where bone and pieces of meat were embedded (Fig. 8*c*).

The relief pictures in Figures 9*a*, *b* and *c* are from the stomach of a man who died of apoplexy a couple of hours after a meal containing meat. The body was formalin fixed as early as one hour after death. The fornix and the upper part of the corpus contained a semifluid mass and air and the greater part of the wall was smooth.

Figure 9*a* shows the mucous membrane in the lower part of the corpus and in the transverse stomach, exposed by an incision through the anterior wall of the stomach. The edges of the incision have been turned carefully aside, and the contents of the stomach have kept in their natural position. In the lower part of the corpus and in the sinus there is visible an irregular, reticulated mucous membrane relief within whose meshes are embedded small bits of meat. In the canalis lies an oval piece of meat about 1.33 by 4 cm. the surface of which is digested to a considerable depth. It is enclosed in a large receptacle occupying the whole breadth of the greatly contracted canalis and extends to the immediate neighborhood of the pylorus.

In Figure 9*c* the large piece of meat is lifted out of its receptacle and is shown on one side of the canalis. On the other side are small bits of meat which lay embedded in shallow chambers beneath the large piece. The large digestive receptacle has formed in such a way that the high relief

FIG. 11. *a*, initial or obliterative relief of a human loop of ileum. The lumen obliterated by folds; *b*, beginning formation of working relief in same loop with digestive chambers of various sizes.

at this site is effaced, leaving a smooth wall except for a few irregular folds at the bottom. Proximally the receptacle is limited by a wall of arcade-like anastomoses between the longitudinal folds in the sinus. A mucous membrane furrow remains open along the greater curvature towards the pylorus.

In Figure 9*b* the large piece of meat has been replaced. We see in this picture that a well-developed longitudinal fold from the lesser curvature projects into the pylorus in front of the meat and in that way bars it from entering the pylorus, yet leaving a narrow, open passage where fluid contents have passed (see Fig. 9*a*) into the duodenum. It is clear that we have here an effective filtering and sorting apparatus.

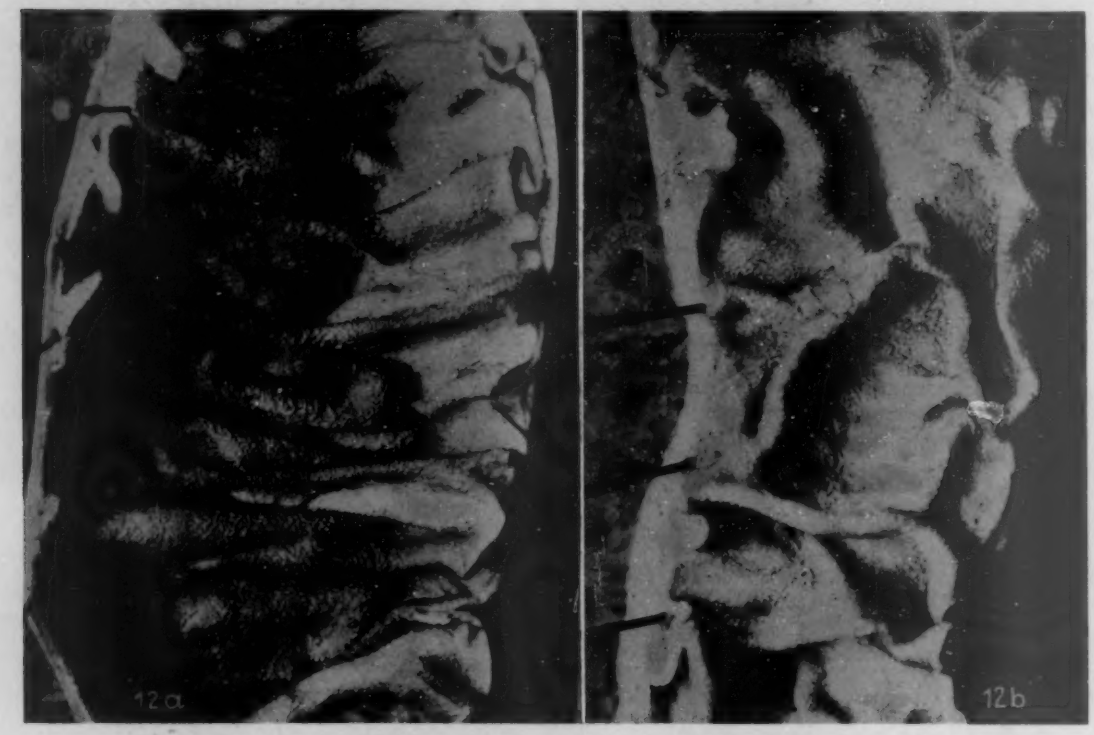

FIG. 12, *a* and *b*. Two types of working relief in the duodenum of a man.

FUNCTIONAL VARIATIONS OF THE MUCOUS MEMBRANE RELIEF IN THE SMALL INTESTINE

In the small intestine, where under normal conditions the contents are fluid and where the solid particles which are emulsified in the fluid are finely divided, the influence of the mucous membrane on the mechanical regulation of digestion can be estimated only indirectly by the effect that its form may be assumed to exercise on the distribution of the contents.

However, in the lower part of the small intestine of a horse, where the finely divided vegetable particles had here and there accumulated into lumps, I observed haustra-like formations surrounded by a wall of mucous membrane folds, enclosing the more solid lumps, or, in other words, an adjustment of the mucous membrane relief in regard to the consistency of the contents. Figure 10*a* shows the relief with and Figure 10*b* without the contents.

Figures 11*a* and *b* show the right and left halves of a high situated ileum coil from a man. In Figure 11*a* the lumen of the relatively wide muscular tube is filled with mucous membrane folds with rich secondary plication. It displays the picture typical of the initial relief in the small intestine. Figure 11*b* presents for the most

part the same relief, but here and there have been formed smooth pockets varying in size. They contained air and very small quantities of liquid. For the rest this coil was empty with the exception of a minimal amount of mucous between the close-lying folds.

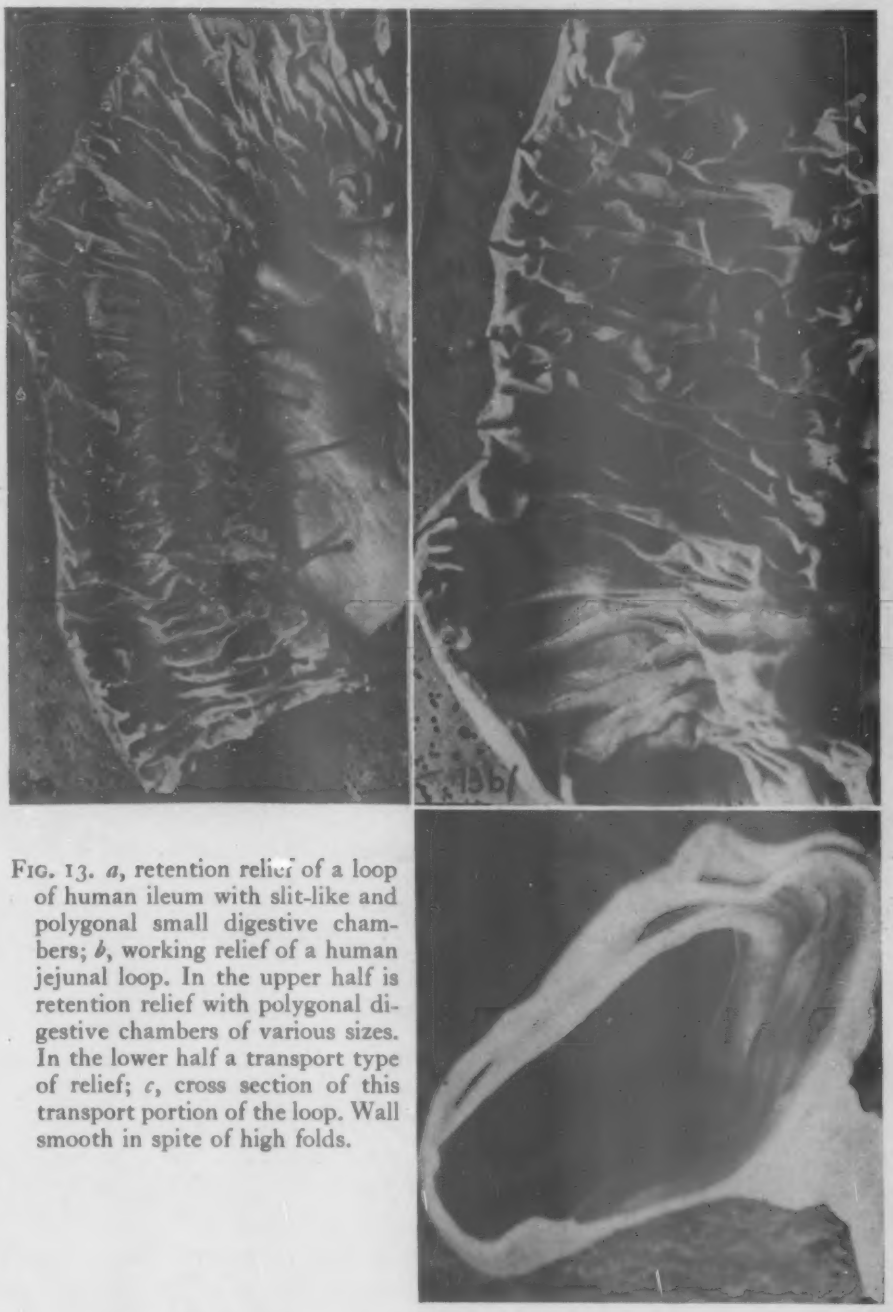

Fig. 13. *a*, retention relief of a loop of human ileum with slit-like and polygonal small digestive chambers; *b*, working relief of a human jejunal loop. In the upper half is retention relief with polygonal digestive chambers of various sizes. In the lower half a transport type of relief; *c*, cross section of this transport portion of the loop. Wall smooth in spite of high folds.

Figures 12*a* and *b* show two mucous membrane relief types from the duodenum of a man. The relief varies greatly throughout the whole of the duodenum. Figure 12*a* displays band-shaped, transverse folds with oblique anastomoses, dividing the lumen into disc-shaped segments. Figure 12*b* presents a honeycomb-like relief which is very common in the duodenum and distributes the superficial layer of the contents in polygonal digestive chambers.

Figure 13*a* shows the mucous membrane relief in an ileum coil, and Figures 13*b* and *c* a jejunum coil, both from man and both containing fluid contents and air. The entire ileum coil and the upper half of the jejunum coil display a high reticulated retention relief with numerous deep digestive chambers. The lower half of the jejunum toward the lumen. Together they form a valve-like arrangement which bars the greater part of the lumen. However, on the convex side of the intestinal tube the mucous membrane forms an open passage, where the intestinal contents, in spite of the great contraction, are allowed to pass in a narrow stream.

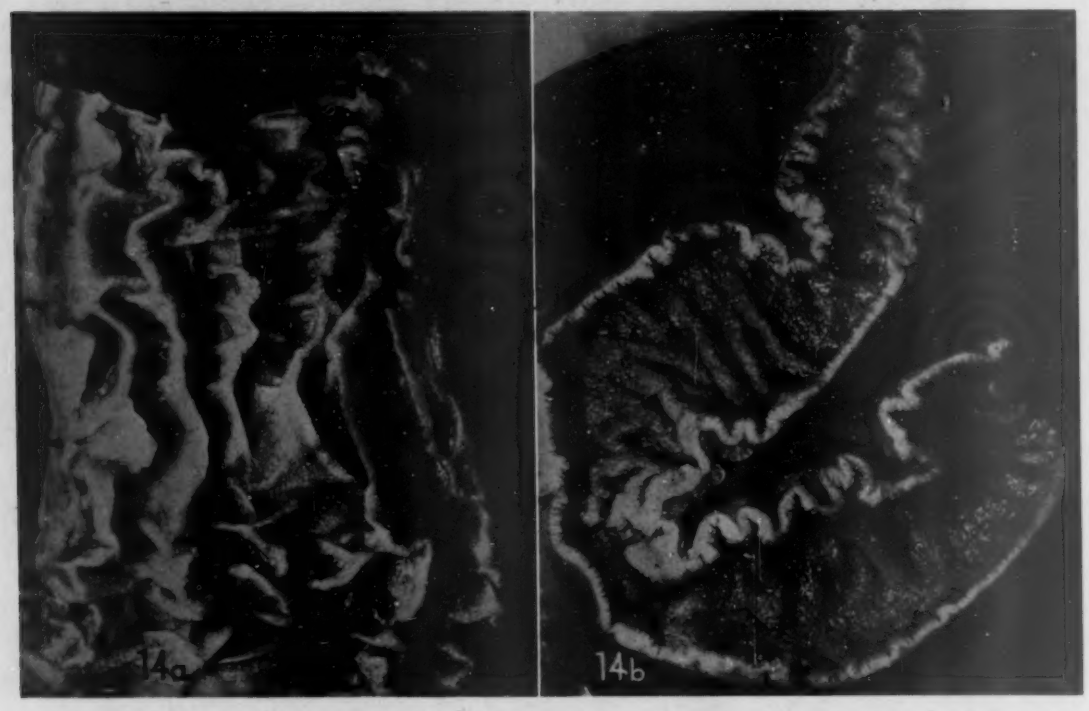

FIG. 14. Functional sphincter and valvular arrangements in the small intestine. *a*, in a human loop of ileum; *b*, in a deeply situated jejunal loop of a monkey (*Tapio sphinx*).

coil (Fig. 13*b*) presents a broad, open, cylindrical lumen. Here high transverse folds cover each other like roof tiles, thus creating a transport form of the relief in spite of high transverse folding (best visible at the transverse section, Fig. 13*c*).

Figure 14*a* presents a straining and barring arrangement with longitudinal folds and fissure-like furrows in an ileum coil from man. Figure 14*b* shows a distal jejunum coil from an ape with a more contracted part between two more relaxed areas. At the site of the contraction the coil is greatly bent with the concavity towards the mesenteric side. Just at the bend a deep muscular contraction, covered by a high wall of mucous membrane folds, rises

FUNCTIONAL VARIATIONS OF THE MUCOUS MEMBRANE RELIEF IN THE LARGE INTESTINE

The part played by the genuine mucous membrane folds in the formation of the internal relief in the large intestine has hitherto been but little noticed. As pointed out in a lecture before the American Roentgen Ray Society fifteen years ago, the genuine mucous membrane folds do play an important rôle in the shaping of the interior surface of the large intestine.

Figures 15*a* and *b* show the mucous membrane relief on the posterior wall of cecum and ascending colon in two apes of the same species (*Tapio sphinx*). In both instances the contents were semifluid. The

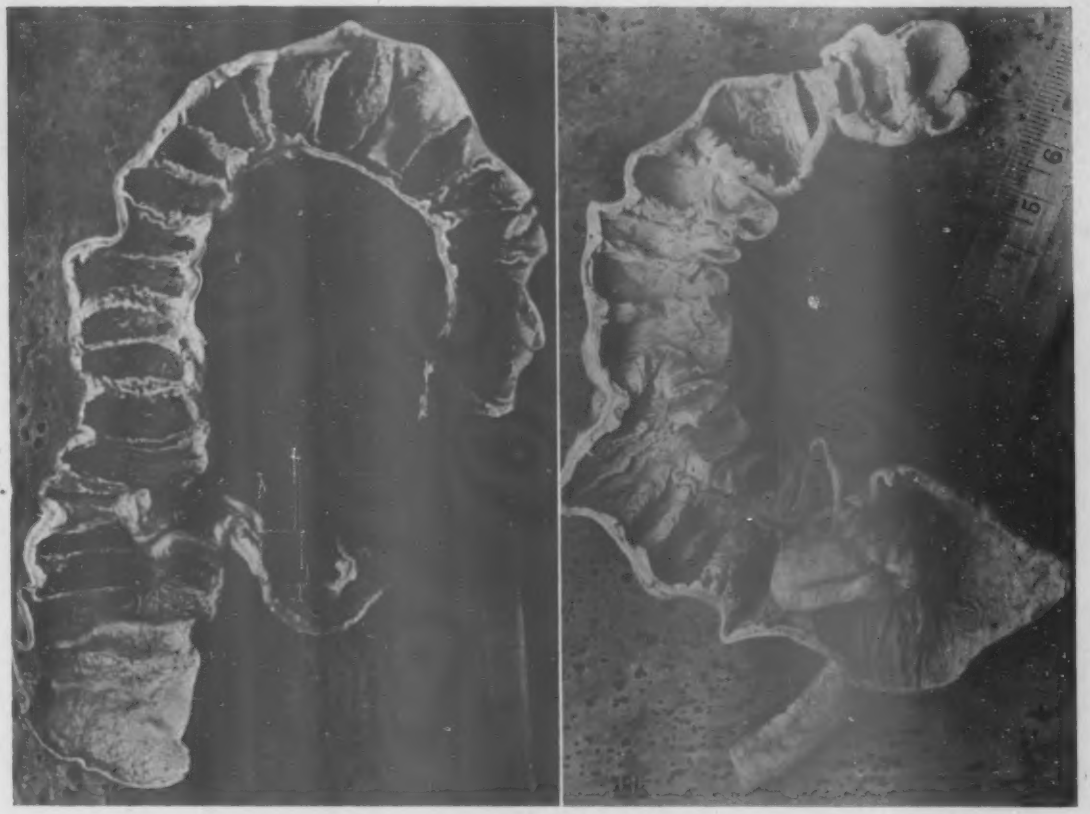

Fig. 15, *a* and *b*. Posterior mucous membrane wall of the ascending portion of the cecum in two monkeys (*Tapio sphinx*). Various types of relief produced by muscle-mucous-membrane folds and genuine mucous membrane folds.

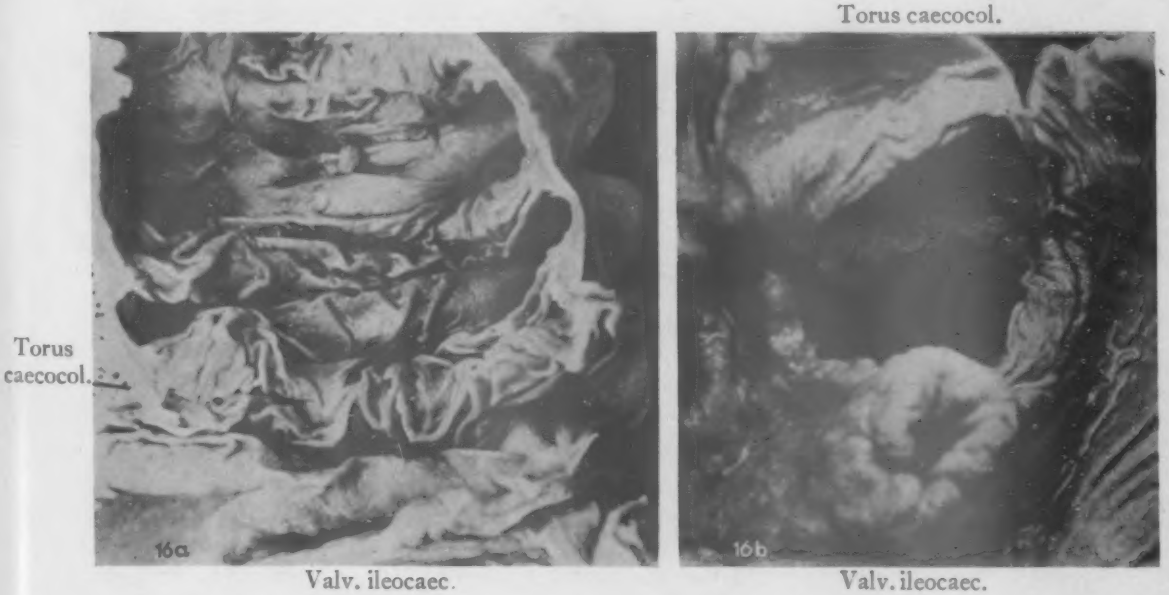

Fig. 16. Cecal bar. *a*, in man, and *b*, in a monkey (*Tapio sphinx*).

upper half of the cecum in Figure 15*a* is divided into haustra by the incisurae semilunares while the lower half is smooth. In Figure 15*b* the cecum is entirely without haustra. In its upper part there is instead a dense mucous membrane relief of anastomosing transverse folds. By the alternate formation of genuine mucous membrane folds and muscle mucous membrane incisurae the cecum can, in a great multiplicity of ways, either form a connected smooth reservoir or else segment the contents into larger or smaller portions.

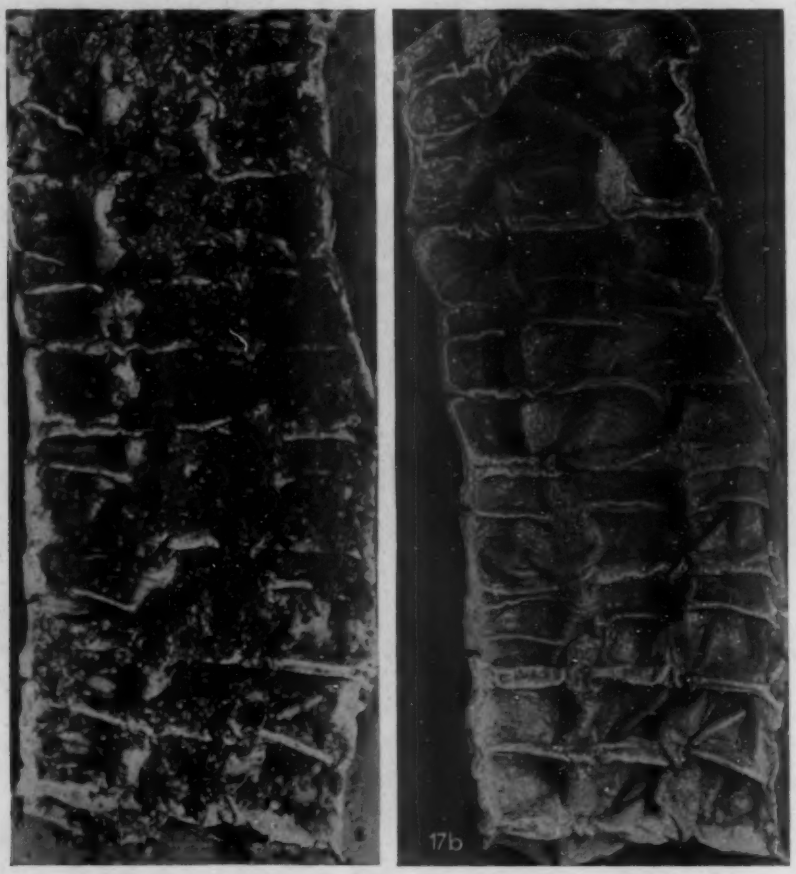

Fig. 17. Distributary and retention relief from the proximal portion of the transverse colon of a monkey. (*Tapio sphinx*). *a*, gruel-like contents distributed in about equal portions; *b*, the symmetrical and similarly shaped mucous membrane pockets, freed from contents.

In both cases a barring formation (torus caecocolicus) in the shape of a strong wall of muscle and mucous membrane separated thin, gruel-like contents in the cecum reservoir from somewhat more consistent—porridge-like—contents in the ascending colon, which, in both instances, is divided into haustra. In the one instance (Fig. 15*a*) this barring wall (T.c.c.) lies on a level with the ileocecal valve and is composed of closely compressed, narrow incisurae semilunares clothed by plain, high mucous membrane ridges. In the other instance (Fig. 15*b*) the bar is situated about 2 cm. higher up, within the lower part of the ascending colon.

Figure 16*a* shows a strong and beautifully built cecum bar in man. The bar consists of three rows of incisurae, which in their natural position were so closely pressed against each other that the haustra

were merely fissure-like. The incisurae are clothed with broad ridges of mucous membrane, formed by means of a network of folds. The entire structure forms a solid ring, 3 to 4 cm. in length. Below it there is visible a broad ileocecal valve.

bar was situated. Similar functional valvular or sphincter-like structures can be formed—and disappear—anywhere in the colon at the borderline between contents of different consistency and between segments of different diameter.

Fig. 18. Retention relief of the distal portion of the transverse colon of the same monkey as in Figure 17 but in a later stage of resorption. *a*, fecal clumps in resorption chambers adapted to their shape and size; *b*, mucous membrane relief after removal of contents.

Figure 16*b* shows an iris-shaped cecum bar (torus caecocolicus) in an ape.

The position of the cecum bar varies with the amount of semifluid contents which are accumulated at the proximal end of the colon. In one instance I have seen a continuous reservoir extend to nearly the middle of the ascending colon, where the

By means of a series of pictures from the large intestine of a species of ape I shall now illustrate two stages in the mechanical regulation of the resorption and the transport of ingesta in the colon.

Figure 17*a* shows the lumen of a part of the transverse colon filled with homogeneous thin, gruel-like contents. Figure

17*b* shows the internal relief of the same segment after the removal of the contents.

We see that the three longitudinal taeniae are contracted, dividing the lumen into three equiform longitudinal channels. Between the taeniae, the incisurae semilunares cut in at regular intervals, producing band-like, straight, transverse walls between equiform chambers ("haustra") resembling dredger-scoops, arranged symmetrically in transverse rows next to each other. Here the mucous membrane forms edges on the muscle septa, varying somewhat in breadth and shape. The picture looks like the interior of a machine intended for the purpose of dividing the whole of the semifluid contents into approximately equal portions for further resorption and desiccation.

In a part of the transverse colon, situated a little nearer the sigmoid flexure (Figs. 18*a* and *b*), resorption has proceeded so far that the contents have acquired a coherent, semisolid consistency. The resorption chambers have now become larger and more irregular in size and shape with semi-

FIG. 19. *a*, rectum and lower portion of sigmoid colon of a monkey (*Tapio sphinx*). The sigmoid colon shows an occlusion or initial relief, the rectum a distention relief. *b*, a human rectum, in the lower part an initial or occlusion relief, in the upper part a transport relief; a muscle-mucous-membrane bar against the sigmoid colon.

spherical, spherical or cylindrical forms. Here the contents have accumulated into rather large portions and have begun to be moulded into fecal lumps. In the formation of these types of retention reliefs the mucous membrane plays a prominent rôle, moulding the semisolid fecal mass into shaped solid scybala.

Figure 19*a* shows the rectum and the lowest part of the sigmoid colon of an ape. Here the colon is greatly contracted and the lumen closed by a high mucous mem-

brane relief. There is no formation of haustra in the muscular wall, but the mucous membrane relief forms three rows of fissure-like haustra (best visible at the longitudinal section of the wall). The closely compressed, broad, transverse walls which limit these mucous membrane haustra, have on their ridges folds in the longitudinal direction of the intestine, which line the central canal, which is closed here. This illustrates an initial relief in the colon with only mucous membrane haustration.

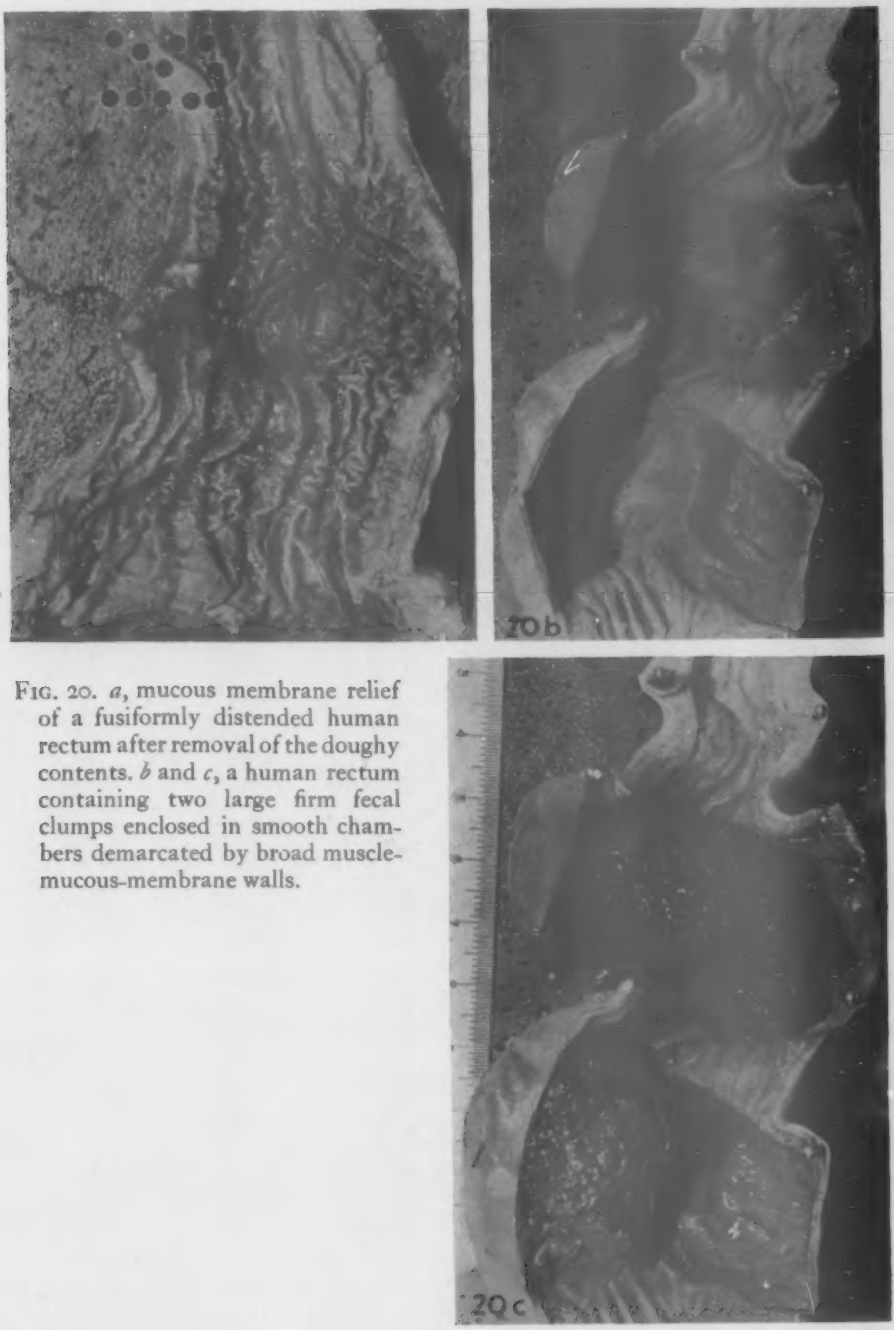

FIG. 20. *a*, mucous membrane relief of a fusiformly distended human rectum after removal of the doughy contents. *b* and *c*, a human rectum containing two large firm fecal clumps enclosed in smooth chambers demarcated by broad muscle-mucous-membrane walls.

The rectum, which was quite filled with

FIG. 21. Mucous membrane relief of the rectum of a horse. Typical scybala chambers.

a cylindrical fecal lump, has a smooth mucous membrane surface with the exception of two very low, transverse muscle folds and some low, longitudinal mucous membrane folds in the ampulla, thus illustrating the rectal distention relief.

In Figure 19*b* the rectum of a man at its lower end is two-thirds empty and is tubularly contracted with the lumen quite filled with high, interdigitating longitudinal folds (the initial relief of the rectum). At the upper part of rectum, the muscular wall is contracted to about the same width as at its lower part, but the mucous membrane folds have here retreated, forming low and irregular longitudinal folds, leaving the lumen open to receive a small amount of feces. The rectum is separated from the sigmoid colon by a circular, contracted part of the muscular wall, fortified by a longitudinally folded mucous membrane bar.

Figure 20*a* shows a human rectum fusiformly dilated and forming a reservoir which enclosed doughy contents. It has a low and irregular mucous membrane relief. Figures 20*b* and *c* show a rectum enclosing two large, solid scybala in smooth chambers, limited by broad and high walls of muscle and mucous membrane folds.

Finally, the multiplicity of the functional

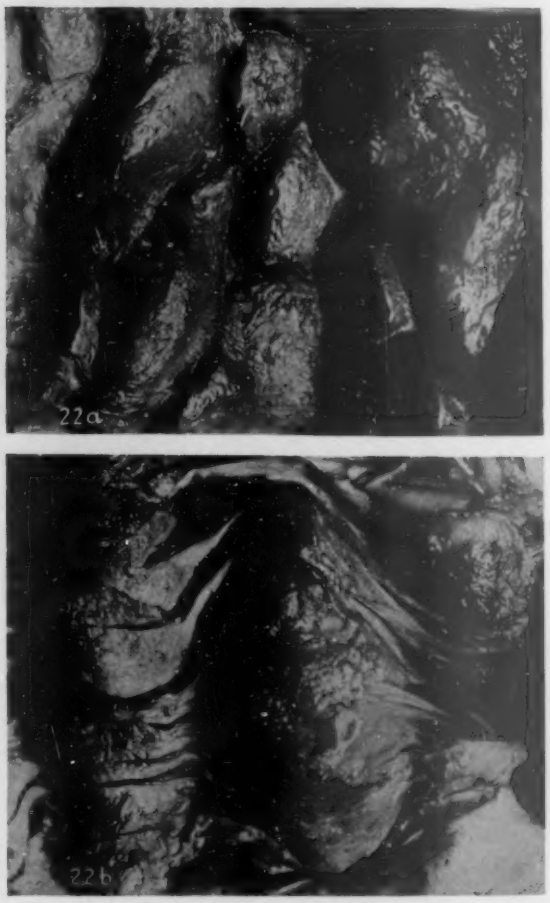

FIG. 22, *a* and *b*. Details of the relief in Figure 21.

variations in form of the mucous membrane is shown by the mucous membrane relief in the rectum of a horse (Fig. 21). Mucous membrane ridges surround polygonal chambers which enclosed the well-known horse scybala.

Figures 22*a* and *b* show beautiful details from the same rectum relief.

CONCLUSIONS

The illustrations which I have shown of the effect of the mucous membrane relief on the distribution and passage of the contents of the digestive canal seem to me to confirm decisively the conclusions respecting the rôle of the autonomous movements of the mucous membrane in digestion to which I came fifteen years ago after studies of the form of the mucous membrane relief in different conditions of contraction in the muscular wall. I shall take the liberty of repeating here these deductions in the way I formulated them in a lecture before the American Roentgen Ray Society in September, 1922:*

The movements of the muscular coat determine the rough division and the large displacements of the contents of the stomach and the intestines. The movements of the mucous membrane produce an extremely differentiated distribution and restraining of the food in digestive chambers of varying form and size, and procure the fine regulation of the current by the passage of the contents in the alimentary canal.

The discovery that the mucous membrane relief in the digestive canal arises by cooperation between the muscular wall and the motor mechanism of the mucous membrane and that the form of the mucous membrane relief is determined by autonomous movements of the mucous membrane, when added to our increased knowledge of the functional morphology and pathology of the relief formations, has made it possible to obtain more reliable and more detailed roentgen diagnoses in lesions of the alimentary canal.

Of still greater medical and general biological importance, however, seems to be the observation that the mucous membrane partakes actively in the mechanical regulation of the work of digestion, for fresh light is thereby thrown on the mechanical regulation of digestion. We have gained a knowledge of a previously unknown mechanism which regulates the work of digestion even to the smallest details in a workshop of delicate mechanism where the machinery is manufactured or altered at any moment or place in accordance with the varying needs of the work of digestion.

* Forssell, G. Studies of mechanism of movement of mucous membrane of digestive tract. Am. J. Roentgenol. & Rad. Therapy, 1923, *10*, 87–104.

SUMMARY

The author reports with the help of serial photographs the results of his continued anatomical investigation of the functional variations in the mucous membrane of the gastrointestinal tract.

His observations on the influence of the mucous membrane relief on the division of contents inside anatomical preparations of the digestive tract fixed *in situ* have confirmed the conclusions in regard to the significance of the mucous membrane movements for the mechanical regulation of the work of digestion which he had already drawn in 1913 from the typical variations in the form of the mucous membrane relief.

CEREBRAL ANGIOGRAPHY BY DIRECT INJECTION OF THE COMMON CAROTID ARTERY*

By FRANK TURNBULL
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CEREBRAL angiography was first described by Egas Moniz[1] in 1927. His procedure consisted of exposing and temporarily ligating the internal carotid artery, and rapidly injecting into its lumen a radiopaque medium. Roentgenograms of the skull were taken at intervals to demonstrate the opaque substance within the homolateral internal carotid and venous circulation. More recently Egas Moniz[2] has advised exposure of the common carotid artery, and injection into its lumen without compression of the vessel.

A method of obtaining intracranial arteriograms and phlebograms by injection through a direct puncture of the common carotid artery was reported by Loman and Myerson[3] in 1936. This obviated the need of operative exposure of the vessel. The technique appeared to offer a solution of one of the objections to cerebral angiography, i.e., open operation.

Direct puncture of the common carotid artery is not a formidable procedure, but neither is it easy. Loman and Myerson approached this new angiographic technique with a unique experience of several hundred punctures of the vessel performed for another purpose. Personal experiences with the method have demonstrated certain difficulties and pitfalls. It will be the purpose of this paper to describe and discuss briefly the procedure in the light of these experiences.

During the past ten years thorotrast has been generally used as the radiopaque medium for angiography. Unfortunately there is a state of doubt regarding the safety of thorotrast injections in the human. A careful study of all available literature regarding the dangers of possible late radioactivity of thorotrast has not impressed me that this is a serious objection to the use of the medium, particularly when not more than 25 cc. is used in the adult. A more cogent criticism is derived from the report of Northfield and Russell,[4] which has recently come to my attention. They described 4 cases in which histological evidence was obtained of retention, after angiography, of thorotrast in the lumen or walls of cerebral vessels. An aggravation of clinical symptoms that was observed in 2 of these cases, and retardation of recovery from operation in another, may have been attributable to this occlusion of vessels by thorotrast. For the present the use of thorotrast, and hence of angiography, appears to to be inadvisable unless exact diagnosis is otherwise unattainable.

In the performance of the "direct" technique of angiography the common carotid artery is punctured at the level of the cricoid cartilage, a point which is usually well below the bifurcation. A $1\frac{3}{4}$-inch, 18-gauge needle, connected by means of a three-way stopcock to a 20 cc. syringe, is used for the puncture. The side arm of the stopcock has previously been attached to an aneroid Tycos manometer by means of a short piece of stiff rubber tubing, which is filled with citrate solution. Once the artery has been entered, blood flows forcibly into the syringe. The stopcock is then turned so that the carotid pressure is transmitted via the citrate solution to the manometer. Regular and wide oscillations of the manometric needle within a range of normal arterial pressure are observed. These indications will ensure that the needle point is deeply within the lumen of the artery. The syringe may then be disconnected and replaced by one containing thorotrast.

In order to slow down the speed of cerebral circulation at this stage, an assistant firmly compresses both internal jugular

* From the Sub-Department of Neurology and Neurosurgery, Vancouver General Hospital. Read at the Seventh Annual Meeting of the Harvey Cushing Society, Memphis, Tenn., April 21, 1938.

veins immediately above the clavicles. Then 12 cc. of the thorotrast is injected as rapidly as possible. The first roentgenogram of the skull is taken at the immediate conclusion of this injection. This film will usually show the internal carotid artery entering the skull and dividing into its branches, the anterior and middle cerebral. Frequently branches of the external carotid, particularly the middle meningeal and superficial temporal, are also evident. The external carotid circulation appears to be about a second or so slower than that in the internal carotid and may not appear on films which are taken the moment that injection is concluded. The blood which flows through the posterior cerebral artery enters the head by the vertebral arteries and consequently this artery does not show in arteriograms. A second roentgenogram, taken four or five seconds after the injection of thorotrast, will outline the venous system within the head, for by then the thorotrast has left the arteries, passed through the capillaries, and is leaving the skull via the veins.

Success in carrying out the necessary maneuvers of this procedure depends largely on well coördinated efforts, not only of the operator but also of his assistant and the roentgenologist. The assistant must insinuate his hands into the field of activity without disturbing the operator. He is able to do this best by kneeling on the table astride the patient. The roentgenologist should be prepared to expose the first film on the operator's signal at the immediate conclusion of injection, and to expose a second film four to five seconds later.

Total injection of thorotrast should be limited to 25 cc. Such an amount will serve for only two injections. If roentgen equipment is available for taking simultaneous anteroposterior and lateral films of the skull, one injection on each side would provide a complete set of roentgenograms. With the apparatus that is ordinarily available, however, one has to decide upon either lateral films of both sides or anteroposterior and lateral films of one side. The two lateral films are generally the more valuable.

Prominent, strongly pulsatile arteries are not necessarily the easiest to inject. They may twist away from the needle like rubber cords. A trial of the direct injection technique is worth while, even though the artery can be barely felt, for in these cases it is often surprisingly easy.

In short-necked individuals allowance should be made for the relatively lower point of bifurcation of the common carotid artery. If exploration with the needle causes an attack of syncope, it is likely that the carotid sinus mechanism has been disturbed. Under such circumstances injection should be attempted at a more proximal level, after a further infiltration of the periarterial tissues with novocain.

To avoid puncture of the internal jugular vein the needle should be advanced in a place perpendicular to the line of the artery or from a point slightly to the medial aspect of this plane. This vein partly overlies the artery, particularly in the lower neck. It may help in making the arterial puncture to exert some lateral traction on the soft tissues of the neck to draw the vein away from the artery. Inadvertent puncture of the vein should be at once apparent on switching the stopcock to the manometer which will show only a slow rise to about 40 and very restricted oscillations of the manometric needle.

A confusing situation can arise if the needle point is not placed deeply within the lumen of the artery and happens to slip out. Blood may collect within the carotid sheath and aspiration still gives one the impression of being in correct position. On switching to the manometer there may be a rise to 80 or 100, with moderate oscillations, but within a few seconds this pressure falls to 40 or less and the oscillations become very slight. When this occurs it is well to withdraw the needle, apply pressure, and defer further attempts to another day.

Two situations which may arise during performance of the "direct" technique

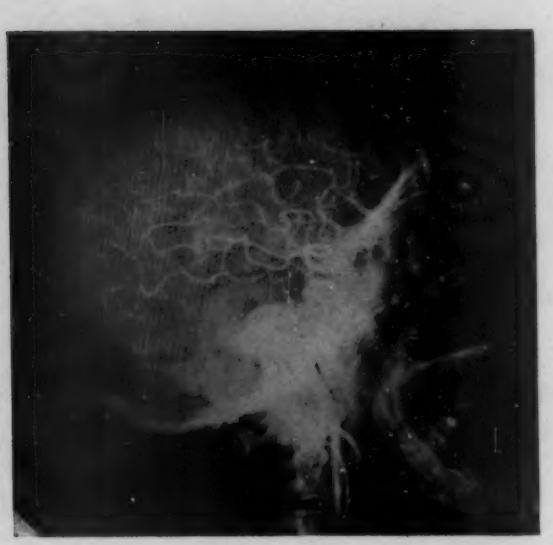

Fig. 1. Case 1. Normal arteriogram showing both internal and external carotid circulation.

cause a considerable disturbance in the intracranial circulation. These are stimulation of the carotid sinus, and repeated obliteration of carotid pulse to arrest hemorrhage when more than one trial is necessary. Under such circumstances it is conceivable that an area of brain which is receiving only a borderline supply of blood may be seriously deprived; or a vessel or aneurysmal sac which is partially thrombosed may become completely obliterated by blood clot.

Interpretation of angiograms obtained after injection of the common carotid artery calls for experience and no little caution. The thorotrast is not as concentrated in the arterial blood stream as when the internal carotid alone is injected. Filling defects should be interpreted with care and only in the light of clinical findings. No precise conclusions can be drawn concerning the caliber of the vessels. Furthermore, the first plate may show most, if not all, of the thorotrast in the external carotid circulation. In clinics where relatively few angiographic studies are required, a close study of the illustrations in Egas Moniz's text, particularly of the normal variations in external and internal carotid circulation, is an invaluable prelude to the interpretation of any of these pictures.

In a study of this method at the Vancouver General Hospital, it has been used on 10 cases. In 7 of these patients, one or both carotid arteries were punctured without any difficulty, and with excellent subsequent roentgenograms. In 3 cases difficulties were encountered. In one of the early cases, thorotrast was injected into the carotid sheath rather than the artery—without causing any harm, but with no thorotrast entering the skull. In a second case, a thick neck and thyroid adenoma made puncture difficult. Two attempts in this case caused carotid sinus syncope and a third resulted in the needle entering the jugular vein. Further trials were abandoned. In the remaining case the common carotid arteries were large and tough, and several attempts at "direct" angiography were unsuccessful. These last 2 patients were strongly suspected of having aneurysms, and in these cases operative exposure of the internal carotid for injection was subsequently used.

CASE REPORTS

Case 1. S. B., male, aged forty-two; admitted April 27, 1937. Clinical diagnosis was tumor of base of skull in right middle fossa. Angiography was done twice on the right side, without causing patient any distress; this on separate days. The first injection was made rather slowly, and roentgenograms taken one or two seconds after injection did not demonstrate the vessels. Pressure was applied to the carotid artery for approximately one-half minute after injection. For several days following angiography there was moderate tenderness over the right side of neck.

The second attempt demonstrated a normal internal carotid circulation (Fig. 1).

Case 11. A. A., male, aged thirty-seven; admitted June 8, 1937. Clinical diagnosis was deep-lying tumor of right temporal lobe. Routine roentgenograms showed abnormal calcification in this area which appeared to outline a tumor. Angiography was done once, without difficulty or causing distress. After removal of needle the artery was compressed for approximately one-half minute. When pressure was released there was immediate forma-

tion of a small hematoma deep in the neck, which caused moderate pain. Some tenderness remained for several days.

The arteriogram showed no filling of the anterior cerebral artery (Fig. 2). The significance of this observation was not apparent. Operation revealed a soft tumor which, because of its position, could not be removed. Post-mortem examination later showed that the tumor, a dermoid, lay on the floor of the skull at the junction of the anterior and middle cerebral arteries. The anterior cerebral artery was stretched over the base of the tumor in such a manner as to completely occlude it.

Fig. 2. Case II. Arteriogram showing no filling of anterior cerebral artery, which was stretched over a tumor.

Case III. T. B., female, aged sixty-two; admitted June 23, 1937. Clinical diagnosis was aneurysm of left internal carotid. Angiography was done on both sides on successive days without difficulty, causing the patient very little distress.

Arteriogram on the right side was normal but on the left side appeared grossly abnormal (Fig. 3). In the left lateral film a vessel which was possibly the internal carotid did not show the usual siphon curve, seemed to be displaced posteriorly, ended bluntly, and gave off no anterior branches. It was felt that this appearance might represent partial filling of an aneurysm containing blood clot. A left subtemporal decompression was done. Later this patient died of a pulmonary embolus arising from a cardiac lesion. Post-mortem examination demonstrated a perfectly normal intracranial arterial tree. On review of this film it is

Fig. 3. Case III. Arteriogram showing a confusing picture related to the external carotid circulation.

evident that the internal carotid artery did not show at all, and that the vessel portrayed was the superficial temporal artery.

Case IV. H. D., female, aged sixty-three; admitted June 26, 1937. Clinical diagnosis was glioma in left internal capsule region. In contrast to previous cases, this patient was stuporous, and somewhat restless when disturbed. Angiography was accomplished on the left side without difficulty. Two successive injections of 12 cc. were made at an interval of ten minutes in order to obtain both lateral and anteroposterior films. About two seconds after injection had been made in both instances there was noted a marked blanching of the whole left side of the face, which persisted about two seconds and gradually faded away. Her clinical condition was not altered.

Fig. 4. Case IV. Arteriogram showing no filling of anterior cerebral artery, which was stretched over a tumor.

Fig. 5. Case vi. Normal arteriogram as far as gross lesion is concerned. Compare with Figure 1.

The anteroposterior arteriogram showed only indistinct filling but nothing significant. The lateral film (Fig. 4) showed no filling of the anterior cerebral artery, a picture which was almost identical with Case ii. Major operation was not performed. Post-mortem examination two weeks later disclosed a large glioma with its anterior two-thirds occupying approximately the same area as Case ii.

Case v. W. M., male, aged forty-six; admitted July 5, 1937. Clinical diagnosis, right frontal tumor. Angiography was attempted on the right side. The carotid artery was of moderate size, easily palpated, somewhat more mobile than usual. Several attempts were made to enter the artery without success. When the vessel was finally punctured, pressure in the manometer showed a slow rise to 100 with only slight and irregular fluctuation. When the stopcock was turned back to the syringe blood could be aspirated readily. Injection of thorotrast entered the carotid sheath. There was no untoward reaction. (Ventriculogram was negative.)

Several months later, at another clinic, cervical arthritis was considered as a cause of his headaches and roentgenograms of the neck were taken. The roentgenologist noted the shadow of thorotrast and very pardonably made a diagnosis of "myositis ossificans"!

Case vi. A. C., male, aged fifty-two; admitted July 7, 1937. Clinical diagnosis was right frontal tumor or subdural hematoma. Angiography was done on the right side. Arterial pulsations were difficult to feel. Injection was accomplished without any difficulty.

Arteriogram (Fig. 5) and phlebogram (Fig. 6) showed excellent filling and no gross abnormality. (Encephalogram showed an extreme degree of irregular cortical atrophy.)

Case vii. G. F., male, aged thirty-seven; admitted August 21, 1937. Clinical diagnosis was possible aneurysm of left internal carotid. Angiography was done on the left side without difficulty. There was some soreness and moderate swelling of the neck for a few days thereafter.

Arteriogram in this case appeared normal.

Case viii. M. F., female, aged forty-eight; admitted June 17, 1937. Clinical diagnosis was glioma of left temporal lobe. Angiography was done on both sides on successive days without difficulty, and causing little distress.

Arteriogram on the right side was normal. On the left side arteriorgram (Fig. 7) showed the branches of the middle cerebral artery to be riding upwards and over some obstruction which could only be a temporal lobe tumor. This was verified at operation.

Case ix. H. A., male, aged thirty-eight; admitted October 19, 1937. Clinical diagnosis was tumor in left parietal region. Bone flap

Fig. 6. Case vi. Normal phlebogram. Note anastomosing veins of Labbé and Trolard.

revealed a condition which was considered to be a subcortical arteriovenous aneurysm. After healing of the operative wound angiography was attempted and was not successful on either side. The arteries were very easily palpable but tended to roll away from the palpating finger. On the right side, the needle slipped out into the carotid sheath as in Case v and on the left side repeatedly entered the jugular vein. (At a later date the left internal carotid was exposed at operation and arteriogram thus obtained showed a large typical arteriovenous aneurysm.)

Case x. H. L., female, aged fifty-one; admitted December 29, 1937. Clinical diagnosis was aneurysm of left internal carotid. This patient was a stout woman with a short, thick neck, midline thyroid adenoma of moderate size, and arterial hypertension. The common carotid artery in the neck was readily palpable. Three trials of direct injection were made: (*a*) Without local anesthetic, and using the usual needle, the carotid artery was approached. Amost immediately after the point of needle reached the neighborhood of the carotid artery, the patient developed severe carotid sinus syncope. Pulse rate dropped to 40, almost imperceptible at the wrist and quite imperceptible in the neck, along with general signs of syncope. This condition persisted for about ten minutes, and no further attempt was made to enter the artery. (*b*) Twenty minutes prior to attempt, 2 per cent novocain was infiltrated along the proposed needle track, and around the carotid artery. A slightly longer needle was used. The internal jugular vein was entered, and attempt to reach the carotid artery was immediately abandoned. (*c*) Preliminary novocain infiltration again. Artery could be easily felt. Several attempts made to enter it, using a short needle, without success. The patient again developed carotid sinus syncope. She was left on table for three-quarters of an hour. The cardiac rate returned to normal but blood pressure remained so low that little pulse could be felt in the carotid. Further attempt to reach the carotid resulted in again entering the jugular vein.

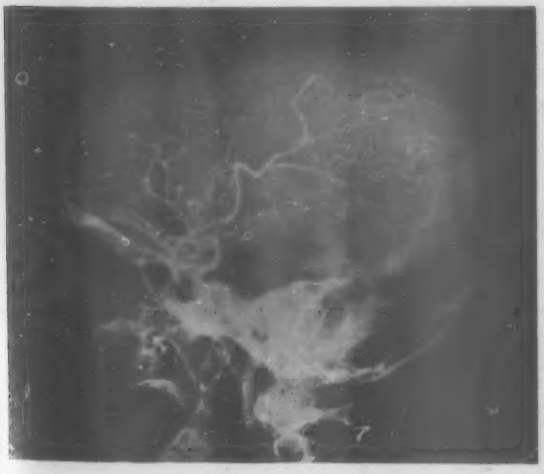

Fig. 7. Case viii. Arteriogram showing "riding up" of middle cerebral branches over a temporal lobe tumor.

Fig. 8. Case x. Arteriogram obtained by injection of exposed internal carotid artery after unsuccessful attempts at "direct" arteriography.

These trials were made on successive days. Following the last attempt she stated that she felt distinctly better. Her most severe symptom, pain over the left eye, was alleviated.

Four days later exposure of the internal carotid artery on the left side was performed under local anesthetic, without difficulty. This artery was punctured and when it was connected with manometer there was normal pressure and the usual wide oscillations. While switching syringes it was noted that the pressure fell to zero. Thorotrast was injected slowly and appeared to meet with obstruction. When the needle was withdrawn there was free hemorrhage from the needle hole. Pressure was ap-

plied about four minutes. On inspection of the internal carotid after this no pulsation was noted. A second injection met with marked obstruction. There was no bleeding from the second puncture hole.

Roentgenograms taken after the first injection showed thorotrast to have been arrested just below the base of the skull (Fig. 8). This patient returned home and has remained (three months) free of her former severe left frontal pain, although she still has diplopia.

It appears likely that the slowing down of circulation in the left internal carotid artery which resulted from her attacks of carotid sinus syncope, as well as from intermittent pressure over the carotid artery in the neck, brought about a clotting of the contents of the aneurysm. The diagnosis is not fully confirmed but the case illustrates the profound alterations in an abnormal intracranial circulation which may result from successive trials of "direct" angiography.

SUMMARY

A technique of cerebral arteriography wherein the end is accomplished without open operation on the neck has obvious advantages. Direct injection of thorotrast into the common carotid artery is not a formidable procedure for patient or operator. It will generally provide a means for making satisfactory roentgenograms of the intracranial vascular tree, both arterial and venous. It is not an infallible method, but its use does not prejudice the success of subsequent operative injection should it be necessary. During performance of direct injection certain technical details must be followed exactly. Filling of the external, as well as the internal carotid circulation provides a minor source of difficulty in the interpretation of films. Repeated pressure over the common carotid artery during successive trials of this technique, or attacks of syncope resulting from the needle stimulating the carotid sinus, may cause profound alterations in an abnormal intracranial circulation. Experiences with ten cases are briefly given.

I wish to thank members of the Department of Radiology of the Vancouver General Hospital who cooperated in this work, in particular Dr. B. J. Harrison, director, and Mr. J. B. Edwards, photographer.

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BRONCHIECTASIS, COLLAPSED LUNG, AND THE TRIANGULAR BASAL SHADOW IN THE ROENTGENOGRAM, AND THEIR INTERRELATIONSHIP*

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BRONCHIECTASIS has been recognized as a clinical entity ever since Laennec's writings of more than a century ago. Collapsed lung, especially that following injuries, operations, and the inhalation of foreign bodies, has occupied a prominent place in medical literature for many years. Triangular shadows at the base of the lungs revealed in roentgenograms, too, have occasionally been described since 1911. These lesions have for the most part been considered as isolated, noninterrelated phenomena. Recent investigations, based both on necropsy findings and on observations of the etiology, nature, and ultimate fate of the triangular shadow in the living over long periods of time, have pointed out a very definite interrelationship of all of these lesions.

Bronchiectasis in circumscribed areas of airless lung, found at necropsy in the lower lobes of children, has caused considerable speculation as to the time and mode of development of the dilated bronchi. Only recently the small basal triangular shadow on pulmonary roentgenograms has been reported as an atelectasis and bronchiectasis of the lower lobe. Previously this shadow, when recognized in children who were acutely ill, was interpreted as pneumonia, later, with milder symptoms, as fluid in the mediastinal portion of the pleural space, in the interlobe, or in the mediastinum, less frequently as an abnormal position of one leaf of the diaphragm or as an unresolved pneumonia of an anomalous or shrunken regular lobe. Inability to secure sufficient fluid by thoracentesis to affect the appearance of the triangular density apparently has finally shaken the belief that large pockets of fluid existed.

Examination of several thousand pulmonary roentgenograms on file at the Children's Memorial Hospital revealed a triangular shadow at the base of either one or both lung fields in approximately 1 per cent. Out of 100 consecutive patients presenting this shadow, 11 died and came to necropsy. In 9, death occurred in infancy within a few weeks after the first pulmonary symptoms. Basing an opinion upon the findings at necropsy in the early cases and a study of the clinical course and serial roentgenograms in other apparently similar patients over long periods, from infancy to beyond childhood in some instances, it seems evident that atelectasis due either to an obstruction of the main bronchus to a lower lobe or of many fine bronchi, usually of the second and third divisions, accounts for the triangular shadow, and under certain conditions is a precursor and not merely an associated finding of bronchiectasis.[1,3,6] Areas of collapsed lung, in this instance the greater portion of an entire lobe, I believe, presage the most common form of bronchiectasis in children. The history of symptoms dating back to infancy does not warrant the assumption common in the past that congenital (malformed) dilatations of the bronchi existed at birth and that atelectasis occurred secondarily. Bronchiectasis of proved congenital origin[2,4] has shown no tendency to involve especially the lower lobes, but the sacculations have been sporadically placed or scattered evenly throughout one or both lungs.

CORRELATION OF CLINICAL AND ROENTGEN FINDINGS

The age of onset of symptoms ranges from a few days to late childhood, approximately 80 per cent occurring in the first

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

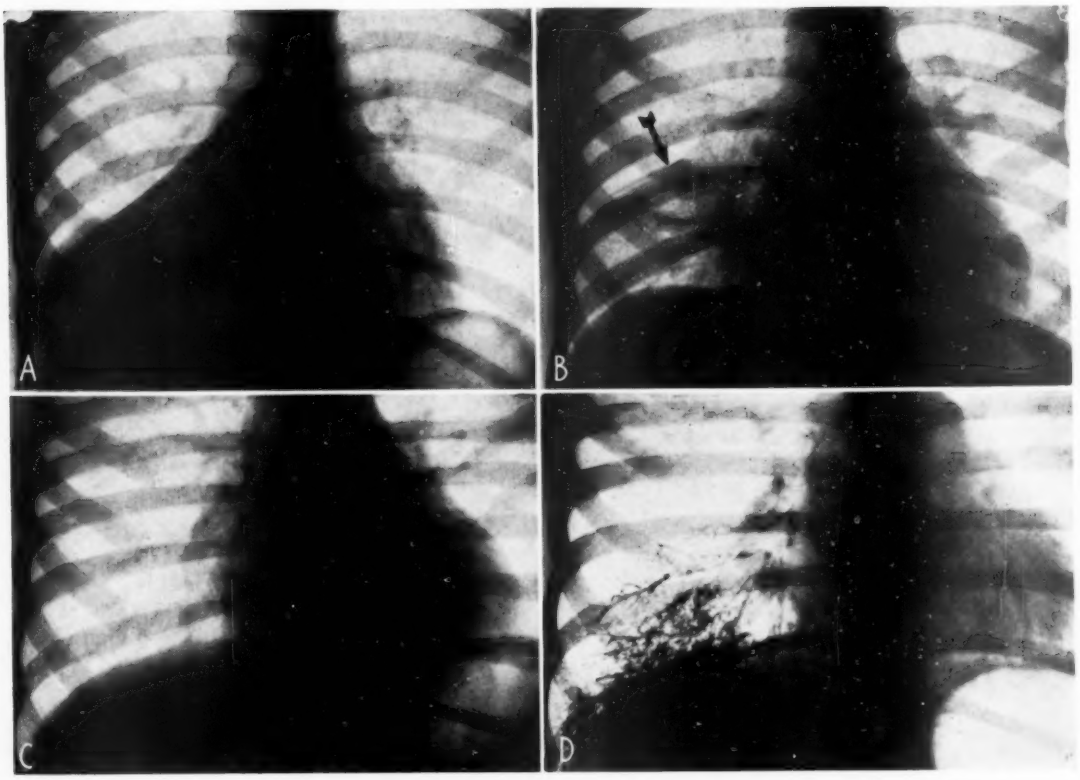

Fig. 1, *A*, *B*, *C* and *D*. D. B., female, aged nine and a half. Early triangular shadow right lung which cleared after removal of thick mucus from bronchus of right lower lobe. *D*, opaque oil fails to reveal evidence of bronchiectasis.

two years of life, rarely in children over five. The first symptoms are usually those associated with infection of the upper respiratory tract. A chill and then a fever of 103 to 105° F. (39.4 to 40.6° C.) makes its appearance, and the condition is commonly interpreted as a lower lobe pneumonia. Roentgenograms made within a few hours after the first acute pulmonary symptoms reveal the small basal triangular shadow which remains long after the disappearance, often sudden, of the severe pulmonary symptoms. A cough, frequently dry at first, later becomes moist, and when this brings the patient back to the physician, it is found that the triangular shadow, which

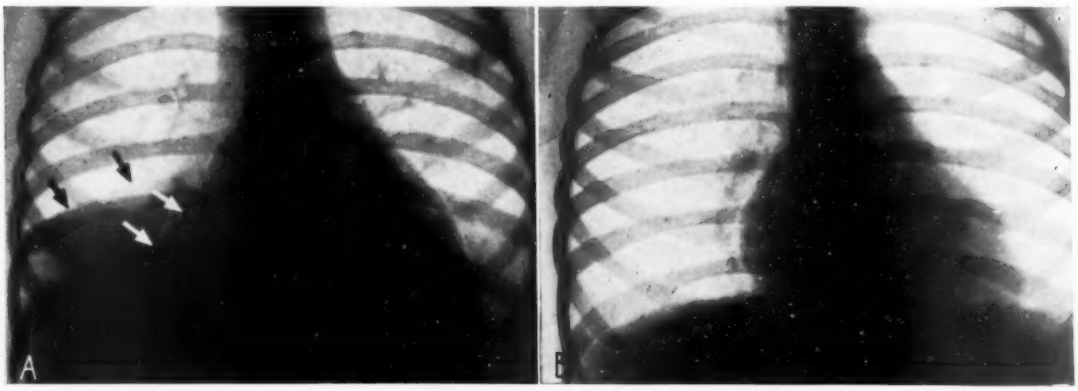

Fig. 2, *A* and *B*. P. G., female, aged six. High-grade collapse of right lower lobe, also partial collapse right middle lobe. Complete clearing after repeated bronchoscopic aspirations.

was noted immediately after the acute pulmonary symptoms, is still present and that the temperature is normal or fluctuates slightly above or below normal. There is frequently a history of paroxysmal cough which, after a time, becomes moist, especially following a sleeping period when the bronchi are not emptied. In cases examined several months after the presence of the triangular shadow, bronchial dilatations are already present. This can be demonstrated by dropping 40 per cent iodized poppyseed oil (lipiodol, also iodochloral), which is opaque to roentgen rays, into the bronchi at the site of the triangular shadow. Sometimes the pulmonary symptoms are so mild for several days after the second or third day, that they are less noticeable than the symptoms produced by the infection of the upper respiratory tract, which is an almost constant associated finding. When drainage is profuse, occasionally secretions spill over from the filled bronchi of the collapsed lobe into neighboring lobes, and additional collapse, often with new shadows on the roentgenogram, takes place, but rarely do any except the most dependent lobules of neighboring lobes remain collapsed over long periods. Bronchophony, bronchial breathing, and crackling râles are present, frequently long before bronchial dilatations can be determined on roentgenograms. Because of this, bronchiectasis is suspected clinically many times before dilatations are noticeable.

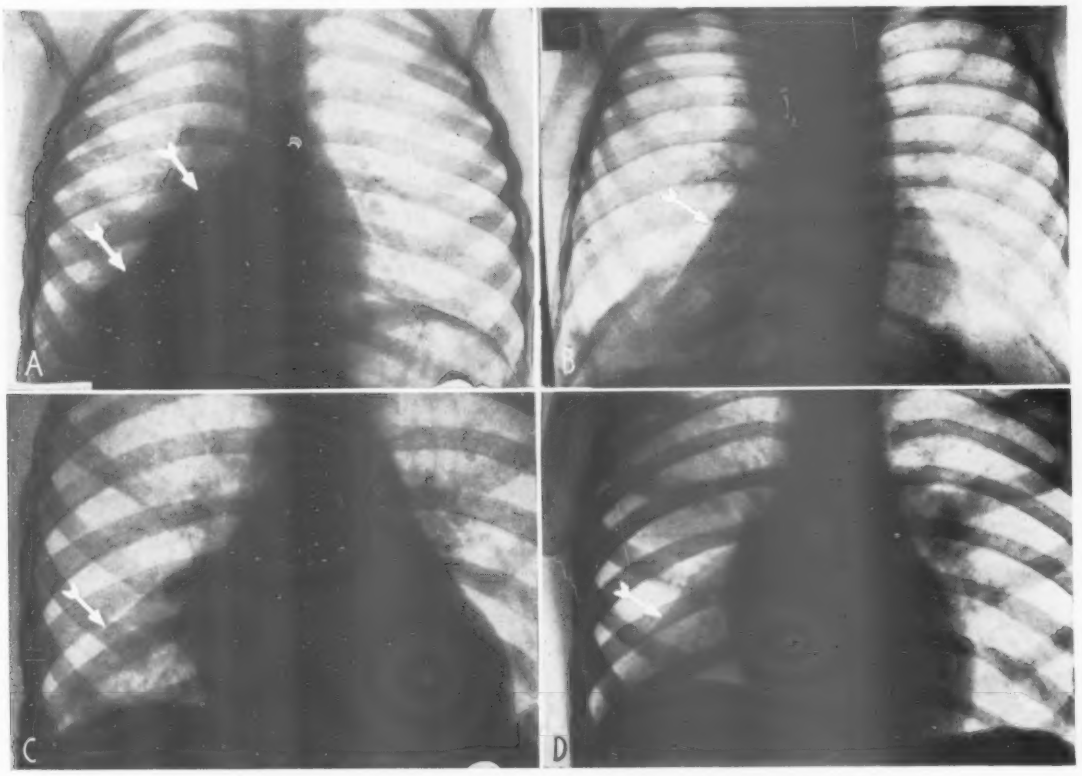

Fig. 3. *A*, D. E., female, aged three and a half; *B*, C. P., female, aged three; *C*, F. G., male, aged ten; *D*, A. C., female, aged seven. A group of 4 cases with varying degrees of persistent atelectasis of right lower lobe. Note how far the heart is drawn toward the affected side.

FLUCTUATING AND NONFLUCTUATING TRIANGULAR SHADOWS

If the triangular shadow shows *marked fluctuations* in size and density from one examination to the next, starting shortly after the acute symptoms of onset, clearing finally occurs without the development of bronchiectasis (Figs. 1 and 2) or with the

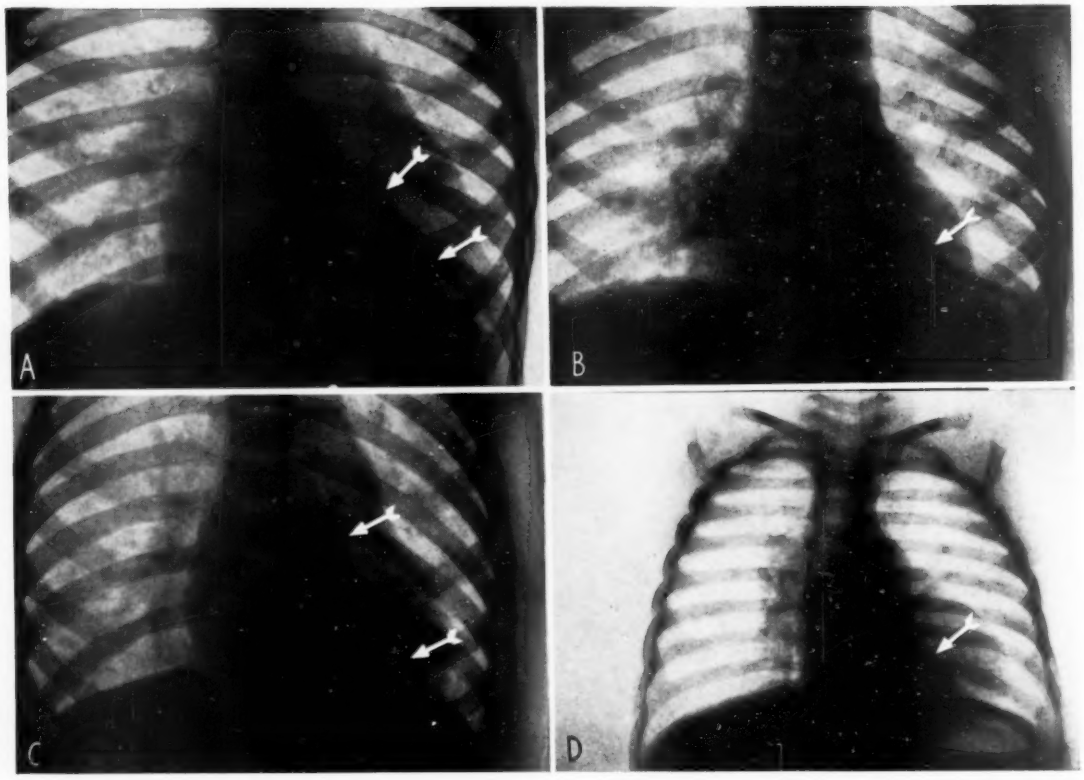

Fig. 4. *A*, M. S., female, aged eight; *B*, A. G., male, aged six and a half; *C*, C. J., female, aged seven; *D*, C. M., female, aged seven months. A group of young children with high-grade collapse of the left lower lobe. Films must be exposed more than usual or the collapsed lobe may be obscured by the heart shadow.

development of tubular dilatations only (Figs. 10 and 11). In this instance, the triangular shadow frequently has slightly

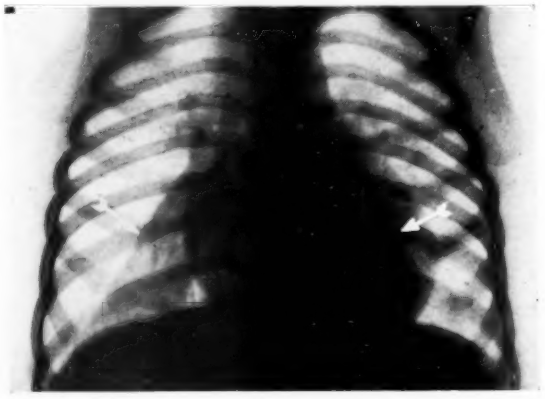

Fig. 5. V. W., female, aged two. Early bilateral triangular shadows (atelectasis of both lower lobes) with right-sided displacement of the heart. Usually when both lower lobes are collapsed the left predominates, lasts longer and practically always pulls the heart to the left.

divergent lines of relatively increased density extending from the hilum to the base, producing a striped appearance. These lines are due to the bronchial walls coated with thick secretion, surrounded by alveoli markedly decreased in size but many still containing a small amount of air. Although the process is prone to last several years, patients with triangular shadows that fluctuate often have a favorable prognosis.

Patients in whom the size and density of the triangular shadows *fail to fluctuate* over long periods develop saccular bronchiectasis (Figs. 12, 13 and 14). Occasionally in advanced cases with large bronchial dilatations, some air reaches the alveoli and there are irregular or circular areas of decreased density within the triangle, but more often the shadow is of homogeneous density. Bronchial dilatations form within a few weeks in the delicate lung tissue of infants,

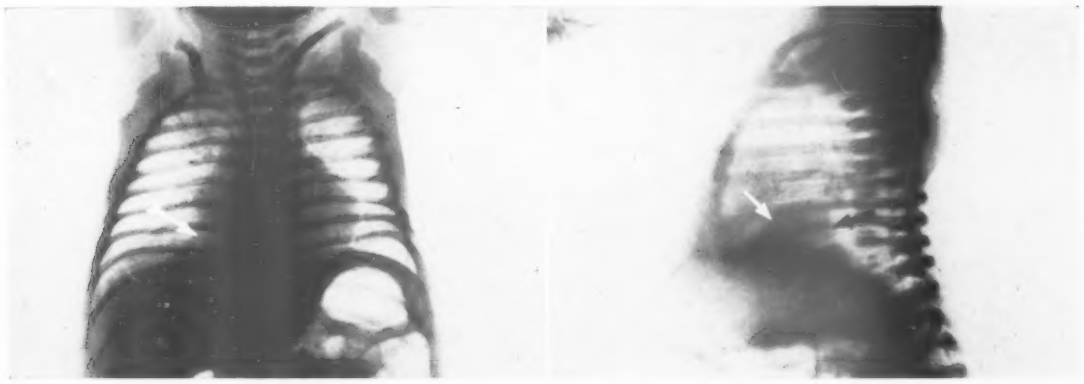

Fig. 6. T. N., male, aged one year. Collapsed right lower lobe not well outlined in the anteroposterior view but is seen as a small dense isosceles triangle in the lateral view pulled in from the costal margin of the thorax. This may be congenital collapse.

but more often six to eighteen months are required for their formation in older children. Older children with *nonfluctuating* triangular shadows survive but younger children, especially infants, often succumb before large dilatations develop.

NECROPSY FINDINGS

Nine patients, in whom triangular shadows persisted on roentgenograms made during life, showed atelectasis of the affected lower lobe at necropsy. In no instance was there noticeable narrowing of the bronchial lumen due to changes in the bronchial wall or to compression from without by enlarged glands or other structures. In the cases of short duration there were no bronchial dilatations. The epithelium, muscle and cartilage were intact, but the smaller bronchi were filled with un-

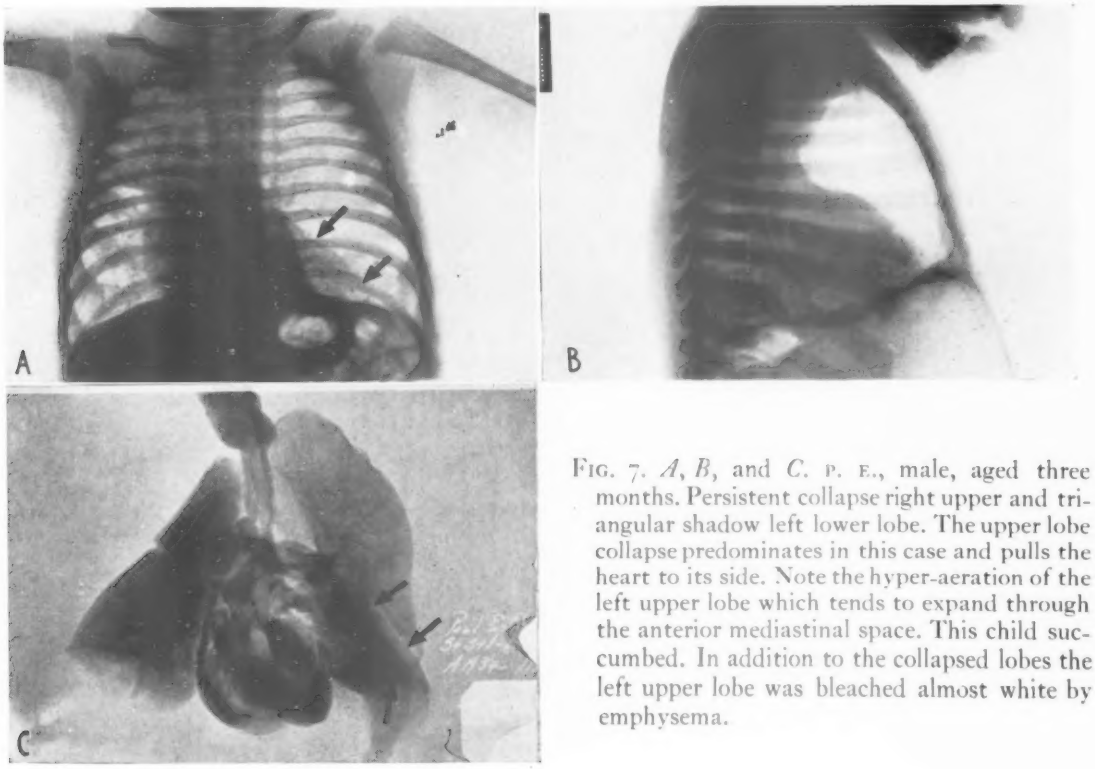

Fig. 7. *A*, *B*, and *C*. P. E., male, aged three months. Persistent collapse right upper and triangular shadow left lower lobe. The upper lobe collapse predominates in this case and pulls the heart to its side. Note the hyper-aeration of the left upper lobe which tends to expand through the anterior mediastinal space. This child succumbed. In addition to the collapsed lobes the left upper lobe was bleached almost white by emphysema.

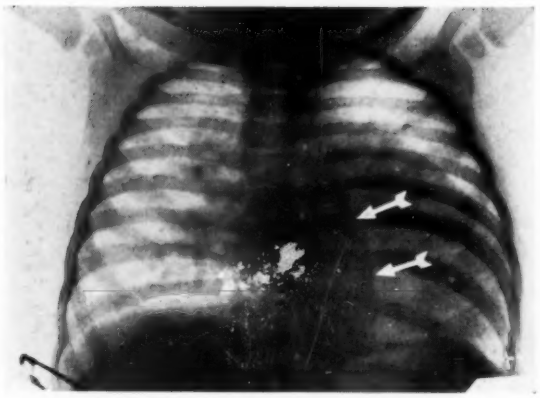

Fig. 8. M. T., female, aged one year. Varying amount of atelectasis of the left lower lobe due to enlarged heart. The size of the shadow seen through the heart fluctuated markedly and pulmonary symptoms were not pronounced at any time.*

usually thick exudate. In cases of a few months' duration, on the other hand, there was swelling of the epithelium together with slight dilatations of the bronchi of the second and third divisions, and often marked infiltration of peribronchial tissues by polymorphonuclear leukocytes. In late cases there were extensive ulcerations and thinning of the walls of the finer bronchi, and widely distributed bronchial dilatations. In cases that developed following an upper respiratory infection or primary infection of the lung, there was no thickening of the pleura or evidence of exudate in the pleural cavity when death had occurred within a year after the presence of the triangular shadow.

* Brennemann, J. Practice of Pediatrics. Pulmonary emphysema. Chap. 52, W. F. Prior Co., Hagerstown, Md., 1937.

PATHOGENESIS

While it is impossible to trace all the factors that enter into the production and maintenance of collapse in an individual case, it seems evident that the major factor is intermittent or continuous complete bronchial obstruction by viscous secretions secondary to infection, to foreign material, or to local hyperplasia of tissue. As the air distal to the obstruction is absorbed by the blood, the alveoli collapse. The collapsed lower lobe is shown by the triangular shadow on roentgenograms. The degree of

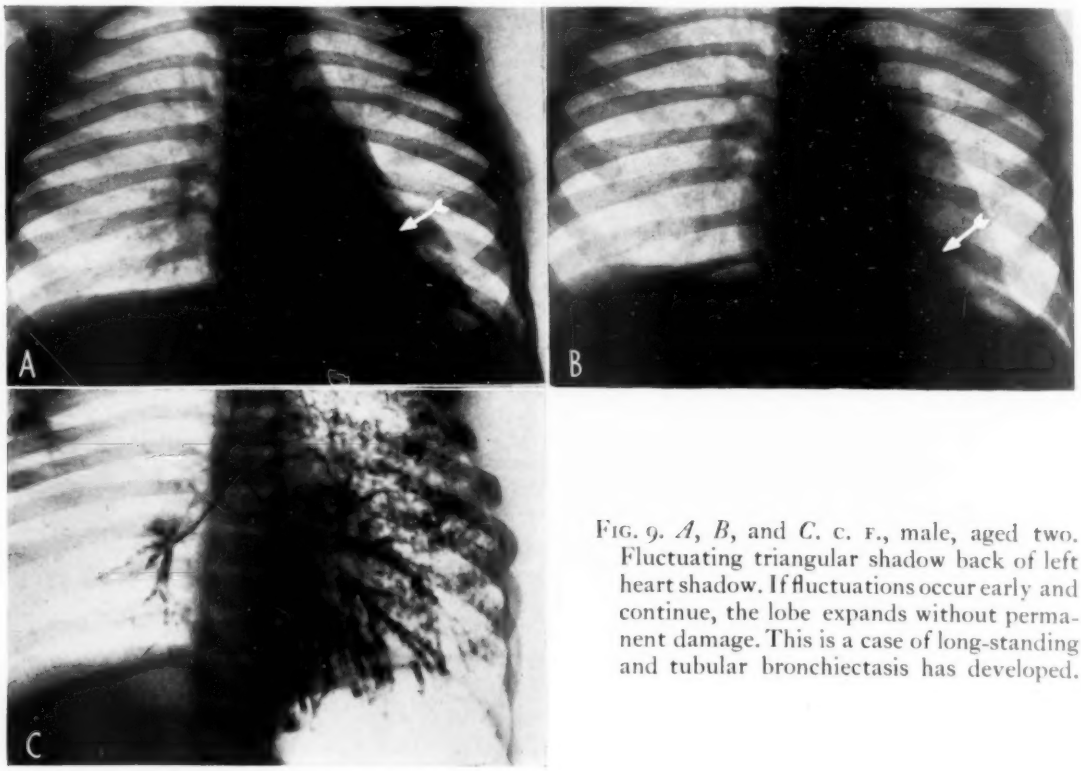

Fig. 9. *A*, *B*, and *C*. C. F., male, aged two. Fluctuating triangular shadow back of left heart shadow. If fluctuations occur early and continue, the lobe expands without permanent damage. This is a case of long-standing and tubular bronchiectasis has developed.

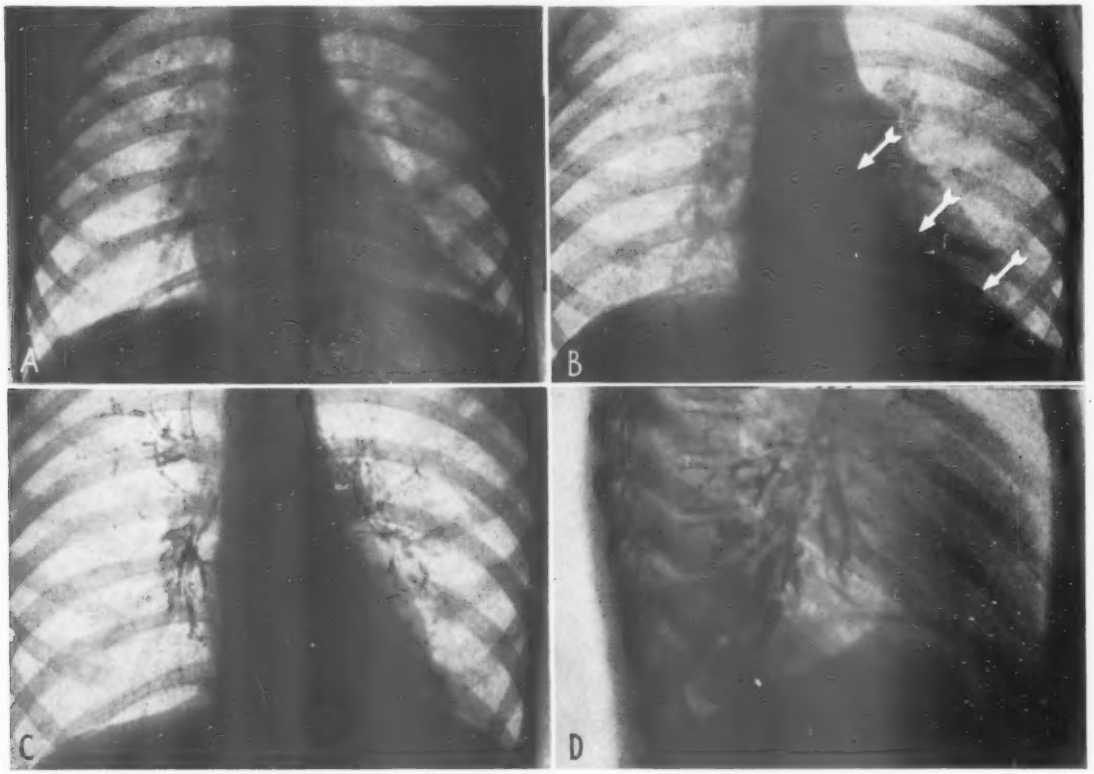

Fig. 10. *A*, *B*, *C*, and *D*. E. A., female, aged six. The first view was taken preliminary to a tonsil and adenoid operation in 1932. The next in 1936 following four years of "bronchitis" with profuse expectoration. The collapse with displacement of the heart is evident. Roentgenograms reveal tubular (possibly fusiform) dilatations of bronchi.

density and smallness of size is directly proportional to the amount of collapse. If the obstruction is incomplete at intervals, air enters and partially or completely re-expands the involved lobe, and, if this is repeated often, either spontaneously or by therapeutic procedures, clearing eventually takes place with no evidence of bronchial dilatations or with only tubular dilatations in cases of unusually long duration. The latter occurs because of a general increase in the fibrous tissue about the bronchi, there being in this instance no marked localized weakening of the bronchial wall. If, on the other hand, a high degree of obstruction persists and there is lack of free replacement of the stagnant infected material collected in the smaller bronchi, by air, re-expansion does not occur and bronchiectasis, saccular in type, develops. This results because of (1) weakness of the bronchial wall due to a long period of fixed position; (2) thinning and destruction of the walls of the finer bronchi by ulceration, the result of retained stagnant secretions; (3) retraction of walls due to marked fibrosis of the peribronchial tissue; and (4) the pull of muscles of inspiration and the elastic recoil of the hyperexpanded neighboring lung tissue. The degree of collapse determines the increase in the intrapleural negative pressure over the normal. This is shown by retraction of the thoracic wall, elevation of the diaphragm, and shift of the mediastinal structure to the affected side.

Foreign bodies in the primary bronchus may cause the production of the triangular shadow. Large foreign bodies prevent to a high degree the exchange of stagnant bronchial exudate for fresh secretions or air from the proximal air passages. Abscesses, as a rule, are formed early, which, because of a communication later with the

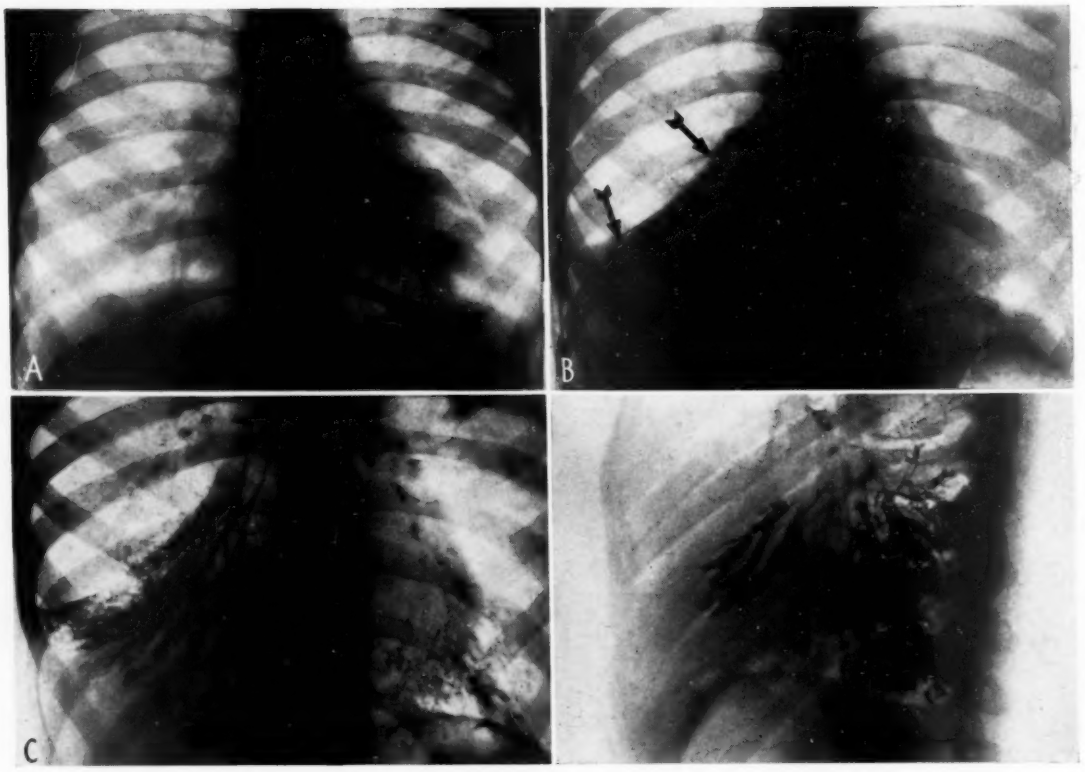

Fig. 11. Patient D. B. *A*, roentgenogram made in 1930 at the age of three years; slightly prominent bronchi to both lower lobes following pneumonia in region of left hilum. *B*, roentgenogram made four years later after profuse expectoration for three and a half years. *C*, opaque oil reveals tubular dilatations throughout the right lower lobe.

bronchi, may leave localized bulbous herniations which have the effect of widened, markedly stretched bronchial lumina. Usually under these circumstances only a few bronchi are involved to a sufficient degree to be demonstrated later as dilatations.

Small foreign bodies, especially particles of food, plus secretions, act like thick secre-

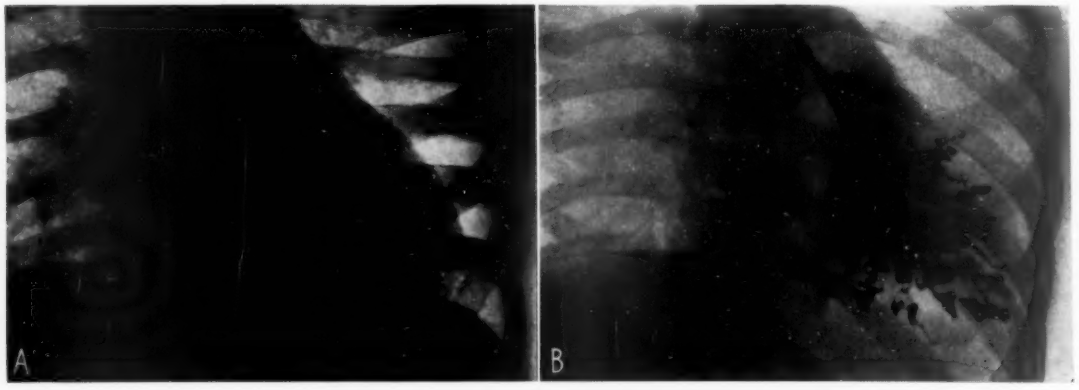

Fig. 12. L. S., female, aged nine. Marked expectoration for six years following "pneumonia." First roentgenogram, *A*, exposed too lightly to show altered density through the heart, but the heart is displaced to the left offering a clue to the diagnosis of atelectasis. *B*, roentgenogram after the use of opaque oil shows many saccules of even size.

tions alone (Figs. 3 and 4). They form a plastic material which makes possible the transmission of the relatively high pressure in the large free air passages to the walls of the occluded bronchi. Better drainage is afforded than with large foreign bodies, and abscesses, pleural exudates and pleural adhesions are seldom met with as complications. During inspiration a pull is evenly exerted upon all of the occluded bronchi. This apparently is the main factor in bringing about the evenly distributed and similar bronchial dilatations throughout all or the greater portion of the lobe.

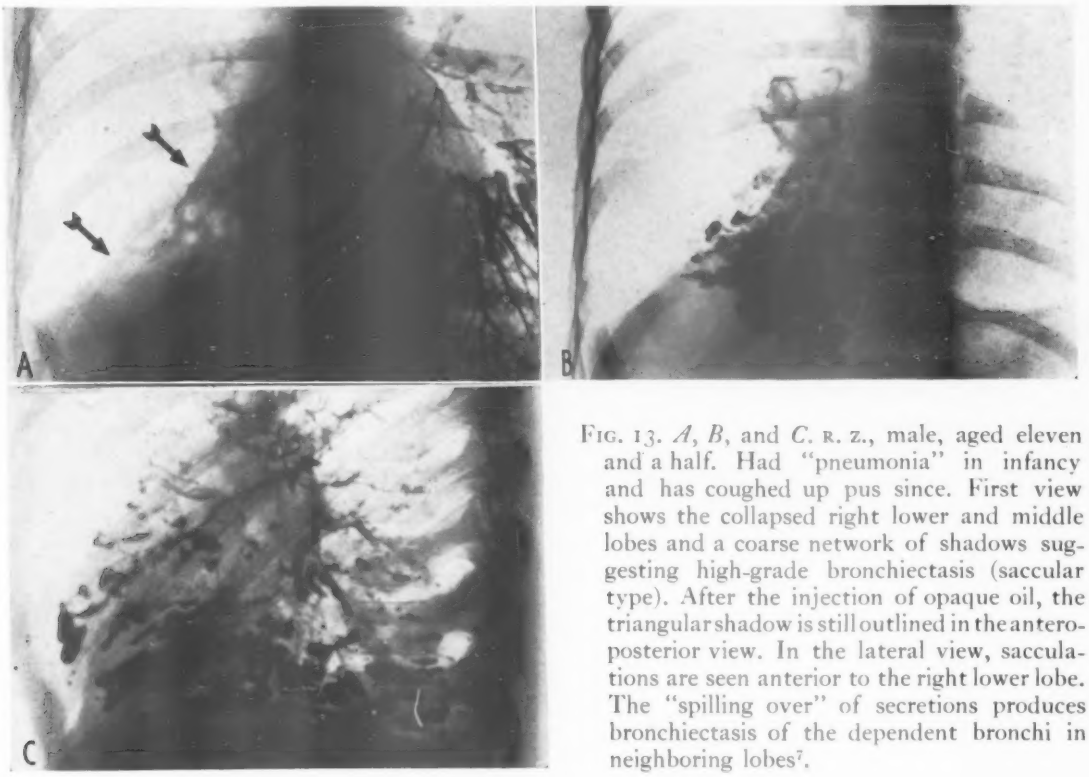

FIG. 13. *A*, *B*, and *C*. R. Z., male, aged eleven and a half. Had "pneumonia" in infancy and has coughed up pus since. First view shows the collapsed right lower and middle lobes and a coarse network of shadows suggesting high-grade bronchiectasis (saccular type). After the injection of opaque oil, the triangular shadow is still outlined in the anteroposterior view. In the lateral view, sacculations are seen anterior to the right lower lobe. The "spilling over" of secretions produces bronchiectasis of the dependent bronchi in neighboring lobes[7].

The triangular shadow, the result of congenital collapse (Fig. 6), is rarely observed immediately after birth, and from all of the evidence at hand one must conclude that practically all lower lobe collapse leading to bronchiectasis develops in postnatal life.

COMMENT

The type of bronchiectasis described here has all rates of development but commonly the bronchi dilate slowly in the absence of abscess formation. Bronchial stenosis plays the most prominent rôle in this disease. In infants and young children thick secretion which is aggravated by infection is the most common cause of obstruction. In older children the bronchi are larger and the evacuation mechanism is more efficient. Collapse at the onset is less frequent. Here a previous insult to the pulmonary system is more apt to have occurred before a significant bronchial stenosis and collapse takes place. These i nsults may be caused by any pulmonary inflammation. When the lumina are sufficiently narrowed or secretions sufficiently viscoid, obstruction and collapse take place.

Because atelectasis occasionally develops following pneumonic consolidation, the question often arises as to the sequence of changes. Marked shrinking does not occur in the presence of the usual type of pneumonic consolidation although the lung may be airless. The alveoli must be fairly normal

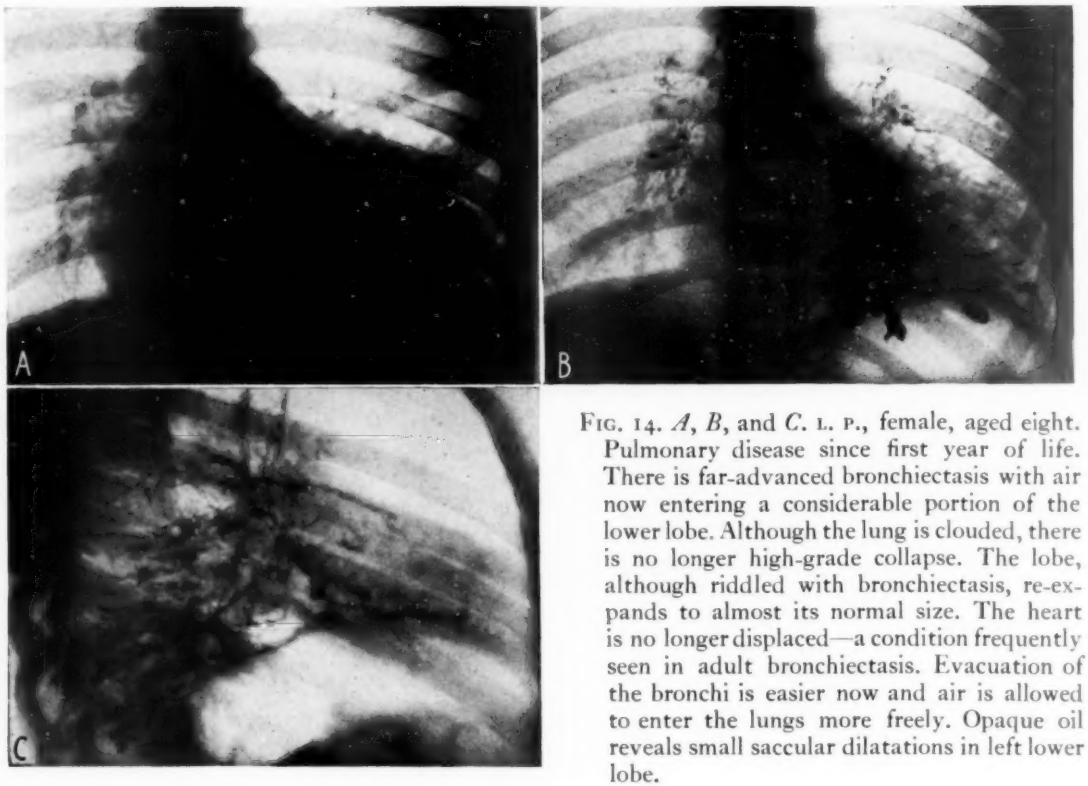

Fig. 14. *A*, *B*, and *C*. L. P., female, aged eight. Pulmonary disease since first year of life. There is far-advanced bronchiectasis with air now entering a considerable portion of the lower lobe. Although the lung is clouded, there is no longer high-grade collapse. The lobe, although riddled with bronchiectasis, re-expands to almost its normal size. The heart is no longer displaced—a condition frequently seen in adult bronchiectasis. Evacuation of the bronchi is easier now and air is allowed to enter the lungs more freely. Opaque oil reveals small saccular dilatations in left lower lobe.

for high-grade shrinking to occur. Atelectasis in older children sometimes takes place following the disappearance of the major clinical and roentgen signs of consolidation.

Routine bronchoscopic aspiration by the specially trained bronchoscopist is of definite benefit. The disappearance of the triangular density has occurred surprisingly soon after bronchoscopic examination even though present for several weeks. In cases in which the atelectasis did not disappear rapidly, the shadows became fluctuating in type and many patients ultimately regained their health with apparently only slight scarring of the bronchi. Occasionally, especially in the young child, an unexpected particle of food or foreign body is discovered. Postural drainage between aspirations has been of definite benefit in older children but has been less efficient in younger children and infants.

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THE ROENTGENOLOGICAL ASPECT OF LUNG EDEMA*

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THE conditions of roentgenological examination of the circulatory disturbances of the lungs are very favorable, owing to the natural contrast between the lung vessels in the lung root and the lung parenchyma and the air-filled alveoli. The discovery of different changes in the filling of the pulmonary arteries and veins permits of reaching important conclusions about the functional condition of the heart.

Passive venous stasis in the lung appears when the blood reflux from the pulmonary veins is deficient. This condition is often observed, the mitral valvular lesions and left heart failure being common and frequent. The roentgen findings in lung stasis and subsequent venostatic fibrosis are particularly well studied in cases of mitral stenosis. In those cases the symptoms of stasis appear without signs of heart failure, due only to the difficulty in the emptying of the lung veins, accompanied by dilatation of lung capillaries and branches of the pulmonary artery.

When heart failure is of short duration, the hypertension in the arterial branches does not appear, because the lung capillary system has at its disposal a reserve capacity. The latter permits of enlarging the bed of lung circulation to such an extent that the excess blood easily finds the necessary space. The experiments of Tojama indicate that the lung has many non-filled capillary ramifications which become filled only in case of greater congestion. Since the circulatory disturbance is prolonged and all the capillaries are overflowed, the pressure in the arterial sector increases and leads to the typical roentgen picture of lung stasis: increased size and density of hilar and perihilar shadows and lung markings. The latter are composed of dilated veins and arteries, the congested capillaries giving the general hazy appearance of the lung fields. The pictures found in pulmonary stasis and its further consequences are well known. On the contrary, pulmonary edema, that is the condition, when transudation through the capillary walls to the lung interstitium occurs, is roentgenologically scarcely studied. The principal cause of this fact is the serious condition of the majority of patients with this dangerous circulatory trouble. In those cases the ordinary roentgen examination is difficult to perform because the patient cannot be transported to the roentgen department. In the last few years, however, the routine roentgen examination has become indispensable to the general practitioner. The bedside roentgen examination increases in frequency and leads to the discovery of many pathological conditions seldom seen in the roentgen department.

As is generally known, pulmonary edema develops when the left ventricle suddenly fails, the right ventricle being functionally adequate. The result is a marked increase of blood pressure in the lung capillary system. The majority of pathologists admit, however, that besides the mechanical factor another factor plays an important part as a causal agent; namely, the walls of the lung capillaries must be altered and their permeability increased. There are many causes leading to this capillary lesion, chronic blood stasis being the principal and most common cause. Other factors of chemical, toxic and vasomotoric nature must be also taken into consideration.

At post-mortem examination the edematous lung is large, heavy, containing little air, and after section a great amount of foamy liquid appears on its surface. Very often pulmonary edema is an agonal condition.

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

FIG. 1. Case 1.

Clinically pulmonary edema occurs in acute or subacute and chronic form. While the description of the clinical manifestations in acute pulmonary edema can be omitted, I should like to stress that pulmonary edema, even of large distention, can be latent, without alarming clinical signs such as great dyspnea, cyanosis, and abundant foamy sputum. The cases without acute circulatory manifestations are of particular interest to the roentgenologist. The acute cases in serious condition present no diagnostic difficulties to the clinician, who then can dispense with roentgen examination. On the contrary, patients with the latent form of lung edema, occurring especially in diseases of the kidneys with hypertension, come sometimes to the roentgen department.

In the radiological literature a few cases of pulmonary edema are mentioned. Day, Sisson and Vogt describe a case of lung edema appearing in a case of anaphylactic shock after repeated injection of antitetanic serum. The condition was of acute character. The patient was examined twelve hours after the culminative moment of dyspnea. The roentgenogram revealed diffuse opacities in the upper portions of the lung fields. The authors suggest that the edema in the lower parts of the lungs had already regressed at the moment of examination. The diagnosis was made after the second examination, twenty-four hours later, when all the opacities disappeared together with the clinical symptoms.

In the case of acute pulmonary edema described by Cola and Otello the opacities, revealed in the perihilar regions of the lung fields, disappeared in forty-eight hours.

In 1934 the French authors Roubier and Plauchu described 4 cases of chronic lung edema observed roentgenogically, occurring in patients with nephrosclerosis and hypertension with azotemia.

CASE REPORTS

From several cases of acute and chronic pulmonary edema the following are of particular interest:

CASE I. W. S., female, aged thirty-two, with mitral stenosis, was admitted to the hospital with acute pulmonary edema. The roentgenogram taken fifteen hours after the clinical symptoms of acute edema ceased (Fig. 1), revealed general reduction of the translucency of the lung fields, on the ground of which large ill-defined areas of densification could be noted. The lung vessels in the hila were dilated. The heart was not much enlarged, but its silhouette was of mitral configuration. The impression at the roentgenoscopic examination was that the lungs contained little air, so that there was no distinct limit between heart shadow and lung fields. It can be compared with the roentgenoscopic image of miliary tuberculosis, where we often cannot distinguish one by one the miliary foci and they give us the impression of insufficient translucency of the lung parenchyma. The roentgen examination repeated after a few days revealed that the lungs were normally aerated.

It is evident that the first roentgenogram corresponded to rests of transudation in the lung alveoli and the interstitial tissue of the lung, however at the time the film was taken the symptoms of acute edema had already disappeared.

CASE II. P. G., male, aged thirty-four, entered the service complaining of dyspnea

and expectoration of blood-stained sputum. Above the dorsal parts of the lungs small moist râles. Urine examination revealed albumin, in the sediment hyaline and granulated casts. The clinical diagnosis was nephrosclerosis with hypertension and uremia, hypertrophy and dilatation of the heart.

The roentgenogram taken immediately after the admission of the patient to the service (Fig. 2) shows enlargement of the heart shadow concerning both ventricles, especially the left, and signs of pulmonary stasis. In the middle part of the left lung and the upper part of the right lung, besides stasis, large diffuse opacities

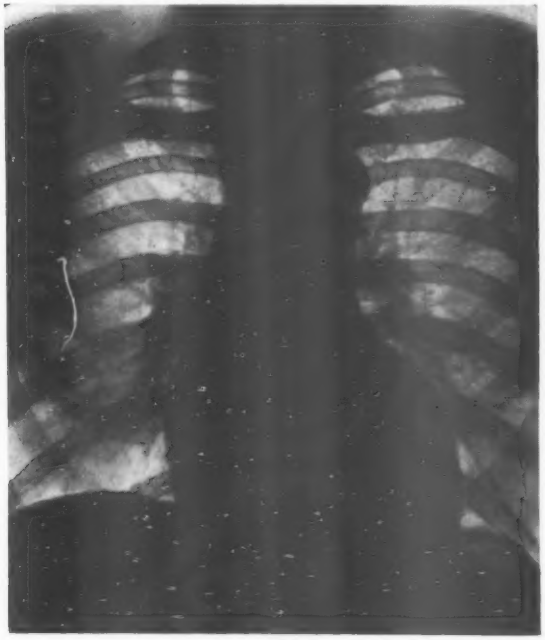

Fig. 2. Case II.

are visible, corresponding to transudation to the lung parenchyma (pulmonary edema). In the lower part of the right pleural cavity there is a small amount of fluid as well as in the upper interlobar space. In this case pulmonary edema was of subacute character and the patient complained only of moderate dyspnea.

The next examination of the patient (Fig. 3) shows only pulmonary stasis. The signs of edema and the pleural fluid have disappeared completely.

Case III. F.W., male, aged sixty-eight, admitted on October 23, 1934. The patient has complained of dyspnea for many weeks. Lately this symptom has grown worse, so that the

Fig. 3. Case II.

patient could not remain in supine position. Tachypnea. The skin pale and humid. Percussion revealed slight dullness in the lower parts of the lungs with rough vesicular sounds covered with sibilant râles and crepitations. The urine contained traces of albumin. The blood urea was 0.7/liter; blood pressure 140/70 mm. Hg; temperature 38° C., the next four days subfebrile and afterwards normal.

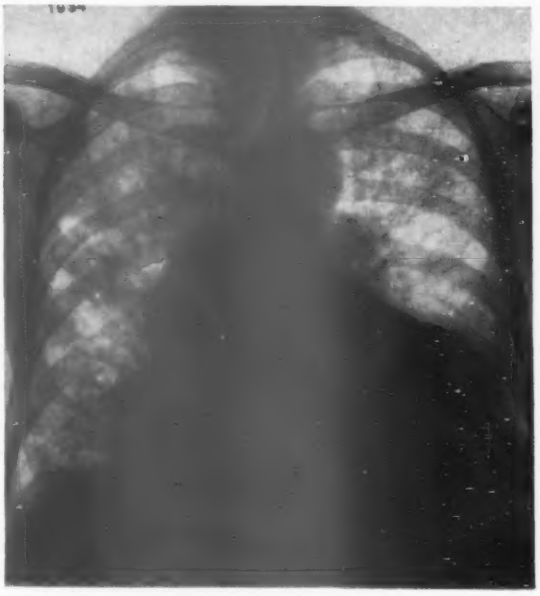

Fig. 4. Case III.

FIG. 5. Case III.

On October 26, 1934, the patient was in a very serious condition. Cheyne-Stokes respiration. Dullness in the interscapular region, respiratory sound rough with crepitations and râles. The roentgen examination on October 10 (Fig. 4) shows great enlargement of the heart dimensions, especially of the left ventricle. Diffuse dilatation of the whole thoracic aorta. A small amount of fluid in the right pleural cavity. Signs of lung stasis with dilatation of hilar vessels. In both lung fields diffuse areolar and confluent opacities are visible. The roentgen diagnosis was lung edema.

Roentgenograms were taken two and five days later and showed that the opacities were now larger in the right lung and diminished in the left one. The last roentgenogram was made on November 7, 1934 (Fig. 5) sixty hours before death. The opacities were confluent throughout both lung fields and the general translucency had notably diminished.

The post-mortem diagnosis confirmed the clinical and roentgenologic findings. Diffuse venostatic induration and marked edema were found in the lungs. In the supradiaphragmatic areas were small foci of bronchopneumonia.

Comment. In this case we had do deal with chronic pulmonary edema in a patient with pulmonary stasis and venostatic induration. The edema occupied at first only certain areas of the lungs, changing its localization and finally involving almost the entire lung parenchyma. No other lung consolidation which could diminish the lung translucency to such a degree was found at autopsy. Therefore we must admit that the roentgen shadows were caused by edematous transudation to the alveolar lumina. The bronchopneumonic foci were very small and confined only to the lower portions of the lungs and of very recent origin. The gradual and slow development of edematous transudation explains the chronic clinical character of the case.

CASE IV. N. M., female, aged thirty-three, with the diagnosis of nephrosclerosis and uremia, hypertension with marked heart hypertrophy and atheromatosis of the aorta. The condition of the patient was very serious; dyspnea, growing worse for ten days, vomiting. The physical examination revealed small bubbling râles in the lower portions of the lungs. In the hilar region tubular breathing. The roentgen examination on September 19, 1934 showed marked enlargement of the heart (Fig. 6) and dilatation of the aorta. In the lung fields diffuse confluent opacities on both sides were visible. The right lung was almost entirely covered with them; on the left side mainly the middle portions were involved. The apices and

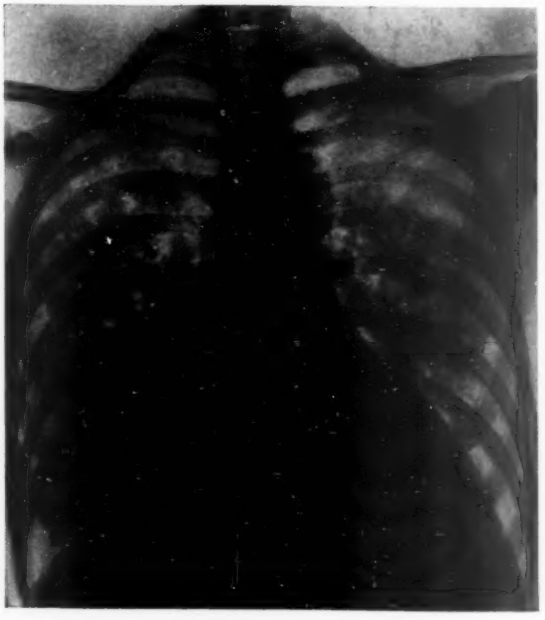

FIG. 6. Case IV.

peripheric regions of both lung fields were still aerated. The roentgen diagnosis was pulmonary edema.

The general symptoms and physical examination did not lead to such a conclusion and clinically only pulmonary stasis was expected, because the clinical signs were not alarming enough. The dyspnea was moderate and abundant foamy expectoration was not present.

On the following days the patient was reexamined a few times. The lung opacities diminished somewhat and on September 24 (Fig. 7) a few opacified areas were yet visible. The hila presented the aspect of lung stasis. The patient felt a little better, the condition still remaining quite serious. Four days after the last roentgenogram the patient died in her home; no autopsy.

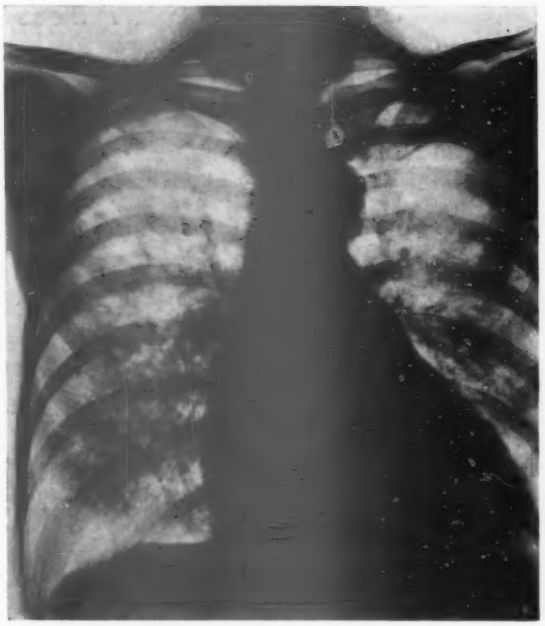

Fig. 7. Case iv.

Comment. In the last case we had to deal with pulmonary edema of subacute character which regressed for some time. The very large extension of the opacities in the lungs, not followed by immediate death, as well as their temporary regression and constant apyrexia speak against confluent bronchopneumonia.

The subacute development of pulmonary edema in the last case as well as in the preceding ones explains the lack of alarming symptoms. In the 3 last cases the causal factors of pulmonary edema were hypertrophy and dilatation of the left ventricle and heart failure resulting from prolonged renal disease.

SUMMARY

From the cases here described the characteristic feature of lung edema is consolidation of large areas of lung tissue, appearing as large ill-defined shadows, confluent and sometimes occupying almost the whole lung fields. Their localization depends on the position of the patient. In patients remaining in a sitting position the lower parts of the lungs are principally involved. When the supine position predominates the middle and even upper parts of the lungs can be affected. The most frequent localization is still the perihilar region. The opacities due to edema are nearly symmetrical in their distribution.

The differential diagnosis must be made between pulmonary edema and confluent bronchopneumonia, the latter, however, seldom attaining so large an extension. The diagnosis can be made after a second examination and by analysis of the roentgenologic and clinical data as well as of the general condition of the patient.

The diagnosis of the chronic form of lung edema, as less known to clinicians, is based mainly on the results of roentgen examination. The last statement deserves to be emphasized.

SOME FRESH ASPECTS OF APPENDICITIS

A JOINT ROENTGENOLOGICAL AND HISTOPATHOLOGICAL STUDY*†

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I. OBJECT OF THIS STUDY

IT IS still doubtful what signs of an appendicular lesion, recognized roentgenologically and verified histologically, can be considered responsible for the complaints of the patients. Some of the anatomical changes that are visible roentgenologically (e.g., kinks, fixations, abnormal position) may represent merely the dry residues of remote disease, or lesions not now in an active stage. On the other hand, pathologists in different countries do not entirely agree as to the interpretation of their microscopical observations. Hence the roentgenological and the histopathological findings in the various manifestations of appendicitis have not yet been completely correlated. In this study, an attempt is made to establish such a correlation on the basis of certain findings, bearing in mind, however, that this method of approach can contribute to the elucidation of one only of the many aspects of the problem.

II. ROENTGENOLOGICAL METHOD

The roentgenological examination of the appendix which we have practiced for the last seven years is part of an examination of the whole alimentary canal. Laxatives are omitted in order to avoid the risk of setting up a colonic irritation indistinguishable roentgenologically from colitis. In severe constipation, a chamomile enema is given the night before the examination.

We use the "simple meal" method: The patient is given a suspension of 30 gm. of unibaryt in 200 cc. of water. After one hour, the regular course of ordinary meals is resumed. Six hours later, the normal appendix should have filled. If it has not, a second dose of the unibaryt suspension is given the next morning and followed by 2 cc. of castor oil. This small dose of castor oil must not be exceeded, for fear of colonic irritation.

With this technique all normal appendices and most of the diseased ones are revealed. The method of observing, obviously, cannot be standardized, because of variability in the shape and position of the appendix, and of the slenderness of its shadow. In general, the technique of Berg has been followed, because of its wide adaptability.

This oral method has given us better results than the enema examination.

III. NORMAL APPENDIX: ROENTGENOLOGICAL ASPECT

In this method, a normal appendix fills completely and uniformly within six hours, provided there is normal passage of the barium through stomach and small intestines. The appendicular lumen is almost cylindrical, temporarily modified by peristalsis. Failure of the appendix to fill at six hours may be due to atony of the cecum, the appendix being filled by the pressure exerted by normal cecal peristalsis. Castor oil, as prescribed above, is known to stimulate cecal peristalsis (Stierlin); very commonly, under this stimulation, an appendix fills normally that did not fill without administration of castor oil.

Unlike its filling, the emptying of the appendix is essentially due to appendicular peristalsis: there are concentric waves (Oppenheimer), or sudden tonic contractions (Knothe), or both combined. Unlike other authors, we were not able to observe that the filling of the appendix is influenced by any type of extra-appendicular peristalsis.

* A preliminary report.
† Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

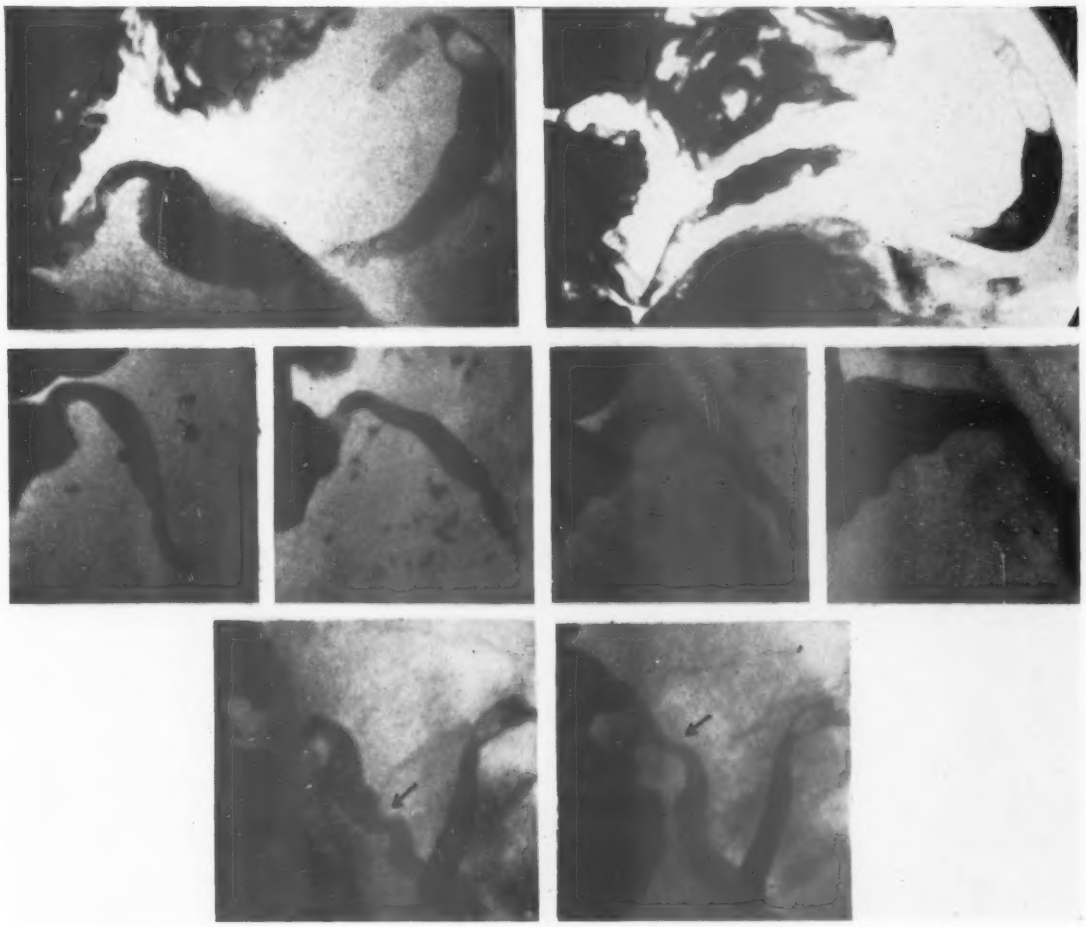

Fig. 1. Peristalsis of the appendix. Roentgenograms taken at twenty-second intervals.

The most active colonic peristalsis, mass peristalsis, does not normally lead to any change in the filling of the appendix; mass peristalsis, in other words, does not help the appendix to empty; usually, it does not even involve the cecum (Oppenheimer). Similarly, stimulation of the colon by enema, injection of pituitrin and administration of prostigmin, do not normally cause any alteration of the appendicular shadow. This is essential in the interpretation of disturbances of the appendicular evacuation, for it shows that interference with normal emptying is due to pathological mechanisms within the appendix.

In all normal persons observed (more than a thousand) the appendix was found empty before the cecum had emptied itself; this takes place at about twenty-four hours. Even severe constipation rarely causes delay in the evacuation of a normal appendix; but, of course, when the filling is delayed by retardation of the passage through stomach and small intestines, emptying also will be delayed accordingly. On the other hand, anomalies of the cecum, such as obstructions or broad adhesions involving the appendix, may retard the evacuation of the latter.

The barium shadow of the appendix is as dense as that of the cecum; it is denser and more homogeneous than that of the ileum. Mobility, usually free, may be diminished when the mesoappendix is short or absent.

In about 10 per cent of healthy persons slight tenderness on palpation over the appendix is elicited at six hours, but is

absent at twenty-four hours. We emphasize these facts because certain authors consider tenderness to be a leading sign in the diagnosis of appendicitis. To sum up: an appendix is healthy when it fills within six hours after the beginning of gastric evacuation, empties before the cecum does, is uniform in caliber, and dense and homogeneous in contrast. Free mobility and absence of tenderness are not essential points.

IV. DISEASED APPENDIX: ROENTGENOLOGICAL ASPECT

Gradually accumulating evidence leads us to expect that particular roentgenological features will prove to be correlated constantly with definite histopathological states. In the course of this conjoint study, which covers a period of three years, a special histopathological type of chronic lesion, hitherto undescribed, has been found to underlie a large number of those roentgen findings which have been previously reported as common in so-called chronic appendicitis. These roentgen signs may be conveniently classified according to anatomical and to functional changes. Concomitant roentgen findings (e.g., ileal stasis, spasms of the pylorus, of the ileocecal valve, or of the cecocolonic sphincter, disorders of colonic mechanics, etc.), although diagnostically important, do not form part of this report.

Anatomically, kinks and fixations, generally taken to be characteristic of chronic appendicular disease, may represent merely fibrous residues of a more or less remote process. Since the evacuation of the appendix may be impeded by coexistent lesions of the appendicular muscular layer, kinks are often associated with stasis in the appendix; but in other cases the appendix empties normally in the presence of kinks. Wherefore kinks and similar deformities are here not considered as evidences of active lesions unless they are associated either with appendicular stasis, or with circumscribed and persistent tenderness at the site of the appendicular shadow, and with disturbances in other parts of the digestive tract.

FIG. 2. Colonic mass peristalsis. Contraction begins in the ascending colon (*X*) and progresses rapidly through the transverse colon, the latter being at this time devoid of haustration. The appendix is not emptied by this movement (arrow); in this case, it emptied itself five hours later.

The mucosal relief of the appendix may be altered in inflammatory conditions. In acute inflammation one may find circumscribed rounded prominences bulging into the lumen; they are from 4 to 8 mm. in length, about 2 mm. high, sharply defined and smoothly rounded; they resemble the tegmina in the neighborhood of duodenal ulcers as described by Forssell. By their persistence, and by their globular outlines, these formations are distinguishable from

peristaltic contractions: they correspond to inflammatory edema of the mucous membrane, and they produce circumscribed narrowing of the lumen. Such narrowing may be caused also by cicatrization of the muscularis or by the presence of abundant adipose tissue in the submucosa; in the former case, however, the constriction is always circular; in the latter, it is less sharply defined and more diffuse than the semilunar prominences caused by edema.

Among the functional signs, retention of barium in the appendix is the most conspicuous. Sometimes associated with cecal stasis, this retention may be due to kinks; but persistent stasis occurs also in appendices which appear to be otherwise normal. In our cases, appendicular stasis was associated with definite histopathological signs of chronic inflammation. These will be discussed later.

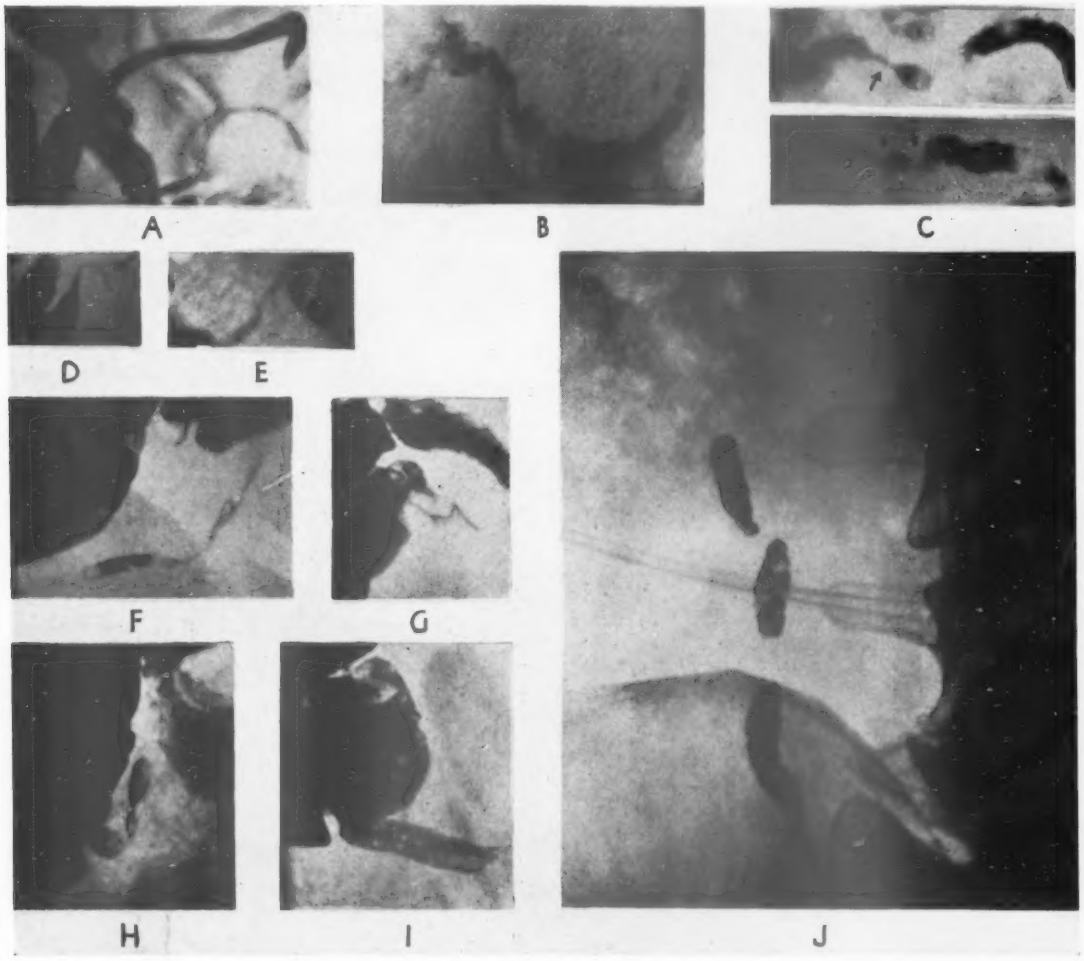

Fig. 3. *A*, normal appendix; *B*, early empyema; *C*, swollen mucous membrane; *D*, acute appendicitis, roentgenogram taken at forty-eight hours; *E*, *F*, *G*, *H*, subacute appendicitis; *I*, mucus in the appendix; *J*, isolated stasis.

In the presence of parasites or fecaliths, retention seems to occur distal to these "foreign bodies," only when chronic inflammation is evident histologically.

Failure of the appendix to fill is now generally believed to be due either to fibrous obliteration or to occlusion of the

FIG. 4. This is the type of stasis here under discussion; only the appendix is filled, but the colon is otherwise empty.

lumen in acute appendicitis. In the course of this study, however, we have observed that traces of barium sufficient to outline parts of the lumen penetrate into the appendix in most cases of acute or subacute inflammation. There may be some delay in this filling, so that such an appendix is not visualized before thirty hours after the barium meal. Without exception, such appendices retained these traces for several days. The discrepancy between our observations and the view previously mentioned is obviously caused by the difference in method.

Catarrh of the appendix is usually associated with catarrh of the cecum or of the whole colon, as evinced by spongy appearance of the barium. Small gas bubbles may also cause this frothy aspect. Usually, the defects in filling caused by mucus are less regularly rounded and more variable in size than those corresponding to gas.

A generalized diminution of the density of the barium filling is often caused by admixture with inflammatory secretion or with pus; the edges of the appendicular

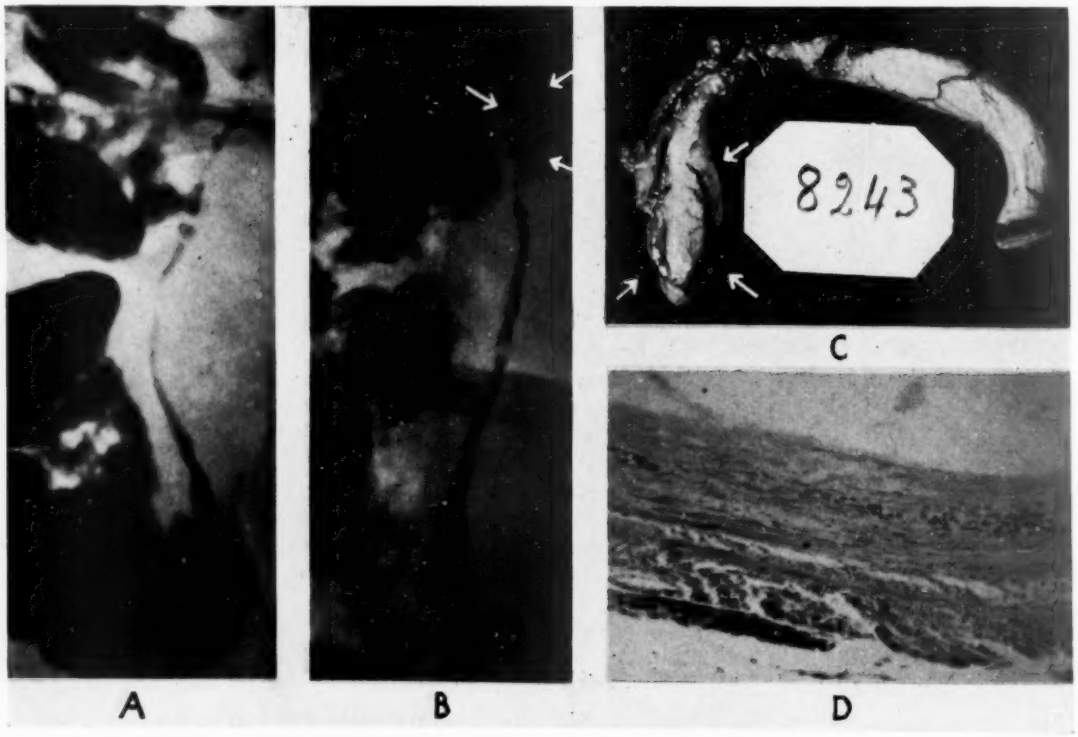

FIG. 5. Appendix at twenty-four hours, *A*, and at forty-eight hours, *B*. Note the increasing dilatation of the tip (arrow). Specimen *C*, and photomicrograph, *D*. Case of chronic appendicitis referred to in the text.

shadow are thereby rendered hazy and ill defined.

Impaired mobility of the appendix may be due to fixation by adhesions; but in 11 cases the appendix appeared almost immovable in the entire absence of adhesions. In these cases diffuse inflammation was found; and it may well be that this impaired mobility was the expression of inflammatory rigidity. On the other hand, free mobility does not exclude adhesions, as these do not always immobilize the appendix completely. Only adhesions at the tip of the appendix are easily discovered by the characteristic straightening which they produce. The common retrocecal position, whether congenital or due to adhesion, rarely escapes observation.

Circumscribed dilatations of the appendicular lumen may indicate hydrops or empyema, but may also occur in typical chronic inflammations without any accumulation of fluid in the lumen. Recently, in 2 instances, we were able to observe the gradual development of such dilatations in the course of an examination extending over two days. Because of the impression that we were watching the development of empyema, we insisted upon immediate operation, whereby the roentgen findings were confirmed, the dilatation being obvious; but microscopical examination did not reveal any signs of beginning empyema, nor of any acute process; it gave, on the contrary, definite proof of a chronic lesion, associated with the type of leukocytic infiltration to be described presently.

As mentioned already, tenderness of the appendix on pressure may be found in healthy persons; on the other hand, it is often absent in typical chronic appendicitis. Tenderness in the right lower quadrant, spontaneous and on pressure, is occasionally found also in acute duodenitis and, rarely, in biliary diseases; moreover, pressure upon the normal appendix may provoke nausea or pain in the epigastrium in patients whose digestive tract is irritable. Because of the proximity of the ovaries, the ureter and the aortic plexus, it is not always possible to determine exactly the actual location of the tenderness. For all these reasons, we do not attach much importance to a finding which, after all, depends chiefly upon the testimony of the patient.

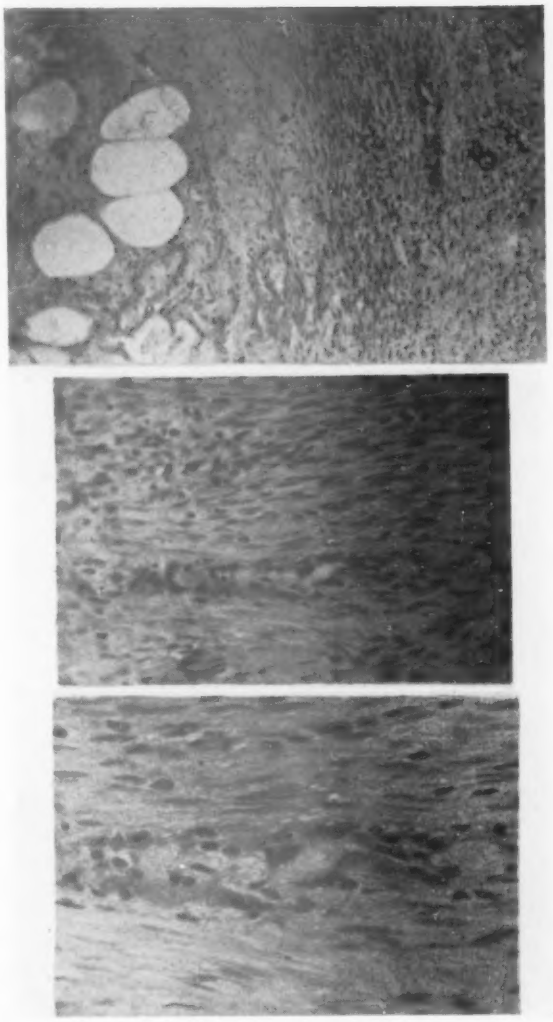

Fig. 6. Photomicrographs of the lesion in the ganglion cells (see text).

ROENTGENOLOGICAL CONCLUSIONS

In appendicitis, whether acute or chronic, stasis in the appendix itself is the leading roentgen sign. This stasis is isolated; barium is retained in the appendix after evacuation of the whole colon or, at least, of the cecum. Appendicular stasis coexistent with colonic stasis is rare and of no diagnostic significance. Even in those acute stages which, by swelling of the mucosa,

caused scanty and delayed filling, stasis was always associated with the other findings.

Filling of the appendix depends upon an extrinsic mechanism; the peristaltic pressure exerted by the cecum forces barium into the appendix when its mouth is open. This is demonstrated by the absence of filling when cecal peristalsis is sluggish, and by its presence after stimulation of such a sluggish cecum.

Emptying of the appendix, on the contrary, is intrinsic in nature, being due to appendicular peristalsis. Normally, there is a balance or complementary correlation of cecal and appendicular peristalsis; in the course of the passage of barium through the colon, cecal peristalsis becomes slower and appendicular peristalsis stronger, whereby the contents of the appendix are forced back into the cecum. Therefore, when the cecum is empty, retention of barium in the appendix must be due to the inability of the appendix itself to expel the barium it contains, and not to any extra-appendicular interference.

Whenever stasis was found roentgenologically, certain histopathological signs of chronic inflammation were demonstrable. This holds true even in the presence of kinks, hitherto supposed to interfere in a purely mechanical way with the evacuation of the appendix. When stasis occurs in such cases, it always coexists with histological signs of inflammation. Appendicular peristalsis being normally as effective as cecal peristalsis, it is hard to see why the latter should be able to force barium past a kink, while appendicular action fails to do so. This discrepancy is explained by the finding of chronic appendicular lesions in all such cases.

Inflammation of the mucosa can be recognized roentgenologically by the swelling it produces. Our observations lead us, however, to lay the emphasis on disturbed intrinsic activity, which, *a priori*, should be correlated with lesions of the muscular layer. The histological findings hereinafter reported furnish the essential foundation on which this view is based.

V. PATHOLOGICAL HISTOLOGY

1. *The Histopathological Technique Practiced.*

(1) Immediately after its surgical removal, the appendix is immersed intact either in 10 per cent formalin solution or in Zenker's formalin, and is kept there for the usual length of time until it is properly fixed. It is better not to slit it open, lest parasites, if present, should be dislodged.

(2) After proper fixation, cross sections are cut from different parts of the entire length of the specimen by means of a very sharp razor, in order to avoid any undue pressure which might dislocate the contents of the lumen. From four to six sections are usually taken.

(3) Sections stained with hematoxylin and eosin are studied; and, when necessary, Leishman's stain is used also.

(4) It has been found advisable to make a systematic study of all the sections prepared and of all the layers, passing from the lumen outward, and noting in order: the contents of the lumen; the state of the mucosa and submucosa, including the lymph follicles; the quality of the submucosal connective tissue; the presence and quantity of submucosal adipose tissue; and, finally, the muscularis and the serosa.

2. *Histopathological Results.*

Practically all of the appendices studied, whether they come from the cadaver or from the living patient, show, on histopathological examination, certain inflammatory reactions which fall naturally into two groups, namely, the *healed* and the *active*.

The Healed Group. This group includes those appendices which show either (*a*) obliteration of the lumen by cicatricial tissue, or (*b*) cicatrization of the submu-

cosa, or (*c*) an increased amount of adipose tissue in the submucosa, or (*d*) scar formation in the muscularis or serosa. No matter what the pathological findings may be, as long as there is absence of leukocytic infiltration in the muscularis and serosa, such an appendix is reckoned as healed.

The Active Group. This group includes those which show leukocytic infiltration in the muscularis. In the study of the sections, as described above, the following details were especially noted:

(1) The Contents of the Lumen: The presence or absence of blood, mucus or pus; of fecaliths or solid particles; of parasites or their ova, or both. None of these findings, by itself, is of diagnostic value, as hemorrhage may be operative; mucus and pus may come from the cecum; parasites and their ova may be found in a healed appendix. Nevertheless, any one of them may occur in active appendicitis.

(2) The Mucosa and Submucosa: These layers are carefully studied as regards the condition of the mucous membrane and the mucous glands, and for evidence of ulceration or exaggerated activity, special note being taken of the following details, namely, the condition of the lymphoid tissue in the submucosa; the presence or absence of inflammatory edema; the character of any leukocytic infiltration that may be present. Positive findings of this kind indicate the presence of a pathological process in the mucous membrane only, but are not sufficient to warrant a diagnosis of appendicitis, this term being used here in the clinical sense. Adipose tissue may be conspicuous in the submucosa. According to some writers, the fat cells are forced into this layer along the course of the blood vessels from the mesoappendix as a result of cicatricial contraction.

The presence of cicatricial tissue in the submucosa is regarded as indicative of a healed lesion, although some of the ganglia of Meissner's plexus may be incorporated in such scars. Hyperplasia of the nerve plexuses, as described by Masson, has not been found by us in all our cases.

When there is a genuine active lesion in the appendix, an active process in the muscularis is a constant accompaniment of the lesions found in the mucosa and submucosa.

(3) The Muscularis: The topographical distribution of the inflammatory process in the muscularis is of special interest. For a thorough understanding of the nature of this process, it is advisable to study the early cases. The results of such a study show the following particulars:

(a) Early in the acute process, when the mucosa shows inflammatory edema and exaggerated activity of the mucous glands, the muscularis shows (*a*) polymorphonuclear infiltration around the blood vessels and similar polymorphonuclear infiltration in the ganglia of Auerbach's plexuses. This is accompanied by degenerative changes in the ganglion cells proper, with vacuolation and cloudiness of their protoplasm. (*b*) Throughout the wall, foci of lymphocytic infiltration. These foci are found irregularly distributed in the muscularis proper and in some of the nerve plexuses of Auerbach, and sometimes also in the serosa.

If the inflammatory process is more severe, the polymorphonuclear infiltration is so intense that the topography above described can be made out only with difficulty; and if it is more extensive, it may invade the serosa, where it can be seen as inflammatory edema or as pus.

(b) When the process is of a milder nature and, for some reason, has been allowed to go on for from five to twelve days before surgical intervention, eosinophiles begin to replace the polymorphonuclears wherever the latter have appeared. This eosinophilia is not easy to explain, as it is only in the appendix that such a phenomenon has been seen, and only in those cases where the attack has lasted for more than four

or five days. There appears to be no close relationship between this process and the presence of intestinal parasites, for, in many of the cases no such parasites were found in any part of the alimentary canal.

In certain cases exhibiting eosinophil infiltration of the muscularis, polymorphonuclear infiltration of the serosa may be concurrent. In such a case, the patient gives a history of two or three consecutive attacks at intervals of three or four days, followed finally by severe localized pain in the right lower quadrant.

(c) Cases of prolonged duration—i.e., anywhere from several weeks to a number of years—without an acute attack, show lymphocytes in the muscularis and, sometimes, in the serosa as well. These lymphocytes are found in small foci irregularly distributed throughout the said layers, often in the neighborhood of blood vessels. They are also found in the plexuses of Auerbach, associated with degenerative changes in the ganglion cells proper, of the same type as that which occurs in the acute and subacute forms of the disease, i.e., vacuolation and cloudiness of the cytoplasm.

It is of special importance to note that foci of lymphocytic infiltration are found scattered throughout the muscularis, and at times also in the serosa, in practically all of the specimens of acute and subacute cases. The significance of this statement—as will be demonstrated presently—is emphasized by the fact that, in our experience, practically all cases of acute appendicitis are actually cases of acute appendicular obstruction.

In considering the factors which may lead to acute appendicular obstruction, the following facts should be borne in mind:

(1) The lumen of the appendix is much narrower than that of the cecum.

(2) The musculature of the appendix is proportionally thicker than that of the cecum.

(3) The filling of the appendix is dependent upon cecal peristalsis provided the appendix is open and relaxed.

(4) The emptying of the appendix depends upon its own mobility.

(5) Pressure in the cecum may force into the lumen of the passive appendix material which the latter can expel only with difficulty. Consequently, when the wall of the appendix is chronically inflamed, whether with scar formation or without it, the existence in that wall of such lesions as have been described above may lead to interference with its mobility and, hence, to obstruction. Obstruction, as is well known, results in necrosis, thus upsetting the balance between the tissues and the microorganisms present, in favor of the latter, and thereby inducing acute inflammation.

This view corresponds to some extent to the results of Aschoff's studies. Direct proof is difficult to obtain. But the correlation between demonstrable motor disturbances and signs of chronic inflammation in the intrinsic neuromuscular system of the appendix is strong presumptive evidence of the correctness of this conclusion. It would seem that a certain type of chronic appendicitis is a common lesion upon which acute inflammation may become superimposed at any time. Hence, when in a case of chronic appendicitis, diagnosed roentgenologically, the question arises as to whether appendectomy is indicated, the answer, in view of the above findings, must certainly be in the affirmative.

SUMMARY

(1) Since the evacuation of the appendix is due to intrinsic appendicular peristalsis only, stasis in the appendix indicates a disorder of intrinsic appendicular activity.

(2) In our observations, stasis confined to the appendix was found to be associated with signs of chronic inflammation in the muscularis of the appendix, especially with lymphocytic infiltration and degenerative changes in the ganglion cells of the plexuses of Auerbach and Meissner.

(3) The same chronic lesion was found in practically all our cases of acute and subacute appendicitis. Correspondingly, in acute and subacute inflammation, stasis in the appendix was observed in all the cases in which some barium had penetrated into the appendicular lumen.

(4) The motor disturbance associated with chronic inflammation seems to be an essential factor in the production of acute appendicitis.

(5) Inflammatory edema, indicative of acute inflammatory swelling of the appendicular mucosa, may be recognized roentgenologically by rounded prominences bulging into the lumen of the appendix.

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RADIOTHERAPY IN HODGKIN'S DISEASE (MALIGNANT GRANULOMATOSIS)

ANATOMIC AND CLINICAL FOUNDATIONS; GOVERNING PRINCIPLES; RESULTS*†

By RENÉ GILBERT
GENEVA, SWITZERLAND

INTRODUCTION

WHEN the President and the Executive Committee of this Congress requested Switzerland to present a report—for which we extend our sincere thanks—I chose the subject which I shall present for two main reasons:

1. To render homage to three American physicians who have the merit of having made and published the first observations of the favorable action of roentgen rays on the adenopathies which characterize Hodgkin's disease: Pusey and Senn, of Chicago (1902–1903), and Williams, of Boston (1902), in whose person I salute a pioneer of medical radiology.

2. To bring to you the fruit of seventeen years of personal experience with a disease to the treatment of which I have devoted special attention as a radiologist.

Malignant granulomatosis (synonyms: lymphogranulomatosis; Hodgkin's disease) is today a morbid entity with well-defined anatomic and clinical characters. In spite of its relatively low frequency, it is decidedly interesting. On the one hand, roentgenologic examination offers invaluable aid in diagnosis, in determining the seat and extent of certain deep lesions, in verifying their regression after treatment or their extension after recurrence. On the other hand, methodical radiotherapy, in the absence of a treatment based on etiologic factors, now constitutes the treatment of choice; although unable to cure the disease, roentgen therapy alone can often bring about long and pronounced remissions as well as an appreciable survival.

By its polymorphism and by the great variation in its evolutionary features in different cases, however, the disease presents great diagnostic and therapeutic difficulties. Its treatment cannot be standardized; it must always be adapted to each particular case and, on the part of the treating physician, requires much clinical sense.

The result to be sought is not the easy and often ephemeral success obtained with a wide variety of techniques on the peripheral manifestations which are so radiosensitive; the aim should always be to obtain prolonged remissions equivalent to clinical cures, remissions which can be renewed without risk on the appearance of the inevitable recurrences.

As a physician, the therapeutic radiologist should be thoroughly familiar with the manifestations of the disease, its types and evolutionary caprices, the ground on which it develops and the reactions of the patient during treatment; it is on these bases that he will select the technique and regulate the dosage, especially with reference to the rhythm of irradiation.

In the first part of this report I shall recall the anatomic and clinical facts which the radiologist should know well because, in spite of the sporadic character of the disease, all the patients in whom a diagnosis is made will be referred to him.

PART I

THE DISEASE

History. In 1832, Hodgkin had the merit of drawing attention to certain patients who presented a simultaneous disturbance of the lymph nodes and spleen. Twenty years later, Wilkes proposed the idea of grouping such cases, however dissimilar

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.
† Translated from the French by Arthur U. Desjardins, M.D., Rochester, Minnesota.

they might appear, under the designation of Hodgkin's disease. Finally, in 1866, Trousseau, in the course of a clinic which has remained famous, described "l'adénie" as a new morbid entity in the great family of diseases affecting the lymph nodes.

Trousseau's description is in good harmony with the condition which the histopathologists were to isolate some thirty years later; but the first effect of anatomic investigations was to complicate the problem; and this confusion ceased only with the work of the Viennese school. In fact, it is to Paltauf and to his pupil, Sternberg (1897–1898), that we owe the description of the histopathologic lesions of this new morbid entity. At last, the diagnosis of "lymphogranulomatosis" rested on solid ground.

In 1904 Benda stressed the "original character" of the granulation tissue present in this disease and proposed the designation "malignant granuloma." This term has the advantage of not implying a specifically lymphoid character; in fact, pathologic foci of the same kind, and with the same histologic structure may be found throughout the mesenchymal tissue of the body.

This is why Ménétrier in his turn advocated the term "malignant granulomatosis."

In my opinion, the expression "Hodgkin's disease," which long served to designate a collection of dissimilar syndromes from which malignant granulomatosis was isolated, should now be employed only with a signification corresponding to the well-defined anatomic and clinical features of the autonomous disease which we are considering.

ANATOMIC AND CLINICAL FEATURES

Anatomic Features. Let us consider successively: (*a*) the lesions of lymph nodes; (*b*) the lesions in other tissues.

Lesions of Lymph Nodes. In the ordinary form of the disease the increase in size of the lymph nodes is the dominant feature. Thus we may find: (*a*) enlarged nodes which are soft and elastic ("rubbery") and which, on section, present islands of necrosis; (*b*) small, hard lymph nodes. Of these two stages which are connected by intermediary states, the former corresponds to cellular infiltration and the latter to fibrosis.

The microscopic appearance varies with the age of the lesion. We may first consider successive phases in an isolated node.

During the early phase, the altered lymphoid structure is still recognizable and corresponds to lymphoid hyperplasia. Then the architecture of the node gradually disappears, and from this point one may observe a multiplicity of cells presenting a pronounced degree of polymorphism; the "giant cells of Sternberg" add a characteristic note to the picture; there may also be observed a proliferation of connective tissue which later will result in the fibrous transformation of the node. This transformation is not complete since, almost always, some granulomatous cells persist. As for the capsule, it is often thickened. Such are the evolutionary stages which may be observed when a single group of lymph nodes is considered separately. When the lymphoid system of a patient is considered as a whole, all the phases described may coexist, even in a single group of lymph nodes removed for biopsy (Gilbert and Babaïantz). Therefore, it is not necessary to depend on the anatomic features to determine the evolutionary stages of the disease.

An essential fact is that malignant granulomatosis presents the macroscopic aspect of a tumor, while its histologic features are those of lymphoid tissue undergoing active inflammatory reaction.

Granulomatous Lesions Outside the Lymph Nodes. Most of the tissues and organs may be invaded by granulomatosis. From an anatomic point of view, those most commonly involved are the spleen (80 per cent of cases) and the bone marrow.

The granulomatous spleen is not necessarily larger than normal; when its volume

is abnormally large, its usually moderate hypertrophy distinguishes it from the major forms of splenomegaly (as in myeloid leukemia, for example). Although its cut surface may appear almost normal, microscopic sections reveal a distorted architecture. To Aubertin and Destouches the involvement of the spleen appeared "metastatic"; in two patients with visceral generalization of the disease, according to Hirschfeld and Babaïantz, it was found histologically intact.

Unknown before Askanazy's description, involvement of the bone marrow may be encountered especially in the vertebrae, then in the flat bones, and finally in the long bones. The diseased foci may reach considerable dimensions. When left to itself, the pathologic process manifests itself by granulomatous infiltration or by compression which destroys the bony tissue. But since, on the other hand, osteoplastic reactions with participation of the periosteum (appositions) are frequent, the risk of vertebral breakdown or of spontaneous fracture is less than in cases of metastasis from carcinoma. The primary focus may be in the medulla of the bone (infectious metastasis) or may arise, by contiguity, from adjacent lymph nodes previously invaded by the disease. The intervertebral discs are respected by the process. Thanks to the structural details which it reflects, roentgenography furnishes a faithful translation of these pathologic changes.

The other organs involved are, in the order of their importance, the lungs (often by contiguity or direct extension from hilar adenopathies),* the pleura (effusion), the skin, the muscles, the central nervous system (especially compression of the spinal cord by invasion of the spinal cord by extension into the spinal canal; possibly myelomalacia by vascular compression); compression of nerves along their course; muscles; then the pericardium (effusion); the upper part of the respiratory tract, the digestive apparatus (including the extrinsic biliary channels), the urogenital apparatus, the organs of special sense, and the endocrine glands.

At the present time, certain rather rare forms, such as primary digestive, pulmonary, or bony lesions without involvement of the peripheral lymph nodes, are known.

The streaked or variegated elements of the granulomatous tissue are found in foci outside of lymph nodes as well as within the nodes. This polymorphism confers on malignant granuloma "an anatomic personality which is complex, it is true, but which is none the less certain and real" (Favre and Croizat).

Pathogenesis. The nature of malignant granuloma has been extensively discussed. So to speak, the disease lies on the divide which separates neoplasms and inflammations (Favre). A tumor by its physical signs, an inflammation by its general and hematologic manifestations, it is regarded today by the majority of authors as an inflammatory disease.

The search for a pathogenic agent has led to many experimental investigations; it may be said, however, that until now a conclusive result has not been obtained. The frequency of latent microbic infection of the lymph nodes has caused many errors of interpretation; the tuberculous origin, which has had many warm partisans, may now be regarded as invalid.

Finally, mention should be made that, by inoculating into the brain of rabbits or guinea pigs a suspension of granulomatous lymph nodes, Gordon produced regularly, after an incubation period of two to six days a pathologic picture (spasms, opisthotonos, then paralysis) which developed in 80 per cent of the experimental animals. However, the introduction of bone marrow seems to induce analogous manifestations (Friedmann†).

According to the gross pathologic lesions observed, the mechanism of extension and generalization of the disease is comparable

* From these specific lesions it is essential to distinguish atelectasis (sometimes lobar) caused by compression of a bronchus by lymph nodes.

† Cited by Bohnenkampf.

to that of an ordinary chronic infectious disease.

The point of entry of the presumed pathogenic agent is not known; the buccal cavity, the tonsils, as well as the upper respiratory and digestive tracts, have been incriminated because of the frequency of the initial adenopathy in the neck, mediastinum and axillae.

CLINICAL FEATURES

General Considerations. Malignant granloma is a sporadic disease which may affect persons of any age and without distinction as to sex; however, it has a strong predilection for middle life (twenty to thirty-five years). Its absolute frequency is greater than was formerly supposed, because it is now more frequently recognized; it is not contagious, familial occurrence is rare,* and 5 female patients have given birth, since the onset of their illness, to 7 healthy children, whose combined ages total forty-three years (extreme ages: two and a half years to eleven years).

Symptoms. Usually the clinical onset of the disease is insidious. The patient feels weak for weeks or months, complains of lassitude, anorexia, loss of weight, and sometimes of fever or pruritus; a slight, commonplace enlargement of lymph nodes, apparently banal and often ignored by the patient, develops usually in the left supraclavicular fossa. In other cases, these slow general prodromes are lacking; the lymph nodes enlarge while the patient is quite healthy, or during the course of an ordinary infection. Exceptionally, the primary focus may be deep (mediastinal adenopathy, slight splenomegaly, or pleural, pulmonary, intestinal or osseous infiltration).

When the disease has reached full development, the peripheral adenopathies are, in the order of their frequency: cervical, axillary, inguinal, more rarely occipital, epitrochlear, popliteal, etc. At the beginning the nodes in only one region are generally involved; then, at a subsequent evolutionary outburst, the disease spreads to other groups of lymph nodes. Painless as a rule, the enlarging nodes may cause "hyperplastic pain" probably due to periadenitis, and more rarely intrinsic pain within the nodes (Chevallier) by distention, the active hyperplasia being resisted by an hypertrophied capsule. Except in rare cases of mixed infections, the nodes never suppurate.

During the first stage of the disease, the most common site of deep adenopathy is the mediastinum; if enlarged mediastinal nodes are to be treated most effectively, their presence must be systematically sought, chiefly by roentgenologic examination, because, even when they are very large, they may be tolerated remarkably well, and only late in the course of the disease may they cause functional disturbances by compression (dyspnea, dysphagia, pulmonary atelectasis) which may progress to the point of mechanical asphyxia.† The volume of the enlarged nodes may vary between that of a hen's egg to that of the heart of an adult human being.

Roentgenoscopically, the contours of the tumor are clear cut, rounded, sometimes polycyclic; the contour outlines do not pulsate. The vertebrae and epidural spaces may be invaded by direct extension.

Enlargement of the hilar nodes may be unilateral or bilateral and may be readily revealed by roentgenologic examination.

Enlargement of the abdominal nodes develops late in the course of the disease (at least, when the disease has begun in some extra-abdominal region); when the mesenteric nodes are involved, they may be easily palpated and are frequently situated in the para-umbilical regions; when the retroperitoneal, periportal or peri-aortic nodes have become diseased, they escape investigation and sometimes are clinically re-

* We have seen one case in brother and sister. The brother, a cheese maker, aged thirty, was the first to become ill in 1924, was not faithful with the treatment, and died in 1927. His sister, who lived nearby, married another cheese maker in 1924, and went to live in another part of France; in her case the symptoms of the disease appeared in 1934, when she was thirty-four years of age. She took treatment and is now in a state of remission.

† In this respect the most dangerous adenopathies are those which develop at the upper opening of the thorax where they compress the trachea.

vealed only by the appearance of ascites or icterus; however, invasion of these nodes occurs rather frequently, and their occult presence should always be suspected when the pathologic process invades the abdominal cavity and its confines.

Finally, paravertebral adenopathy may manifest itself by erosion of bones made visible by roentgenography, but often spontaneous or induced pain may be the only local index. In such cases I always resort to careful palpation of the spinal column, with the patient lying recumbent and relaxed so as to locate the suspected areas with greatest accuracy.

Splenomegaly, when present, is moderate and painless as a rule; it recedes after roentgen therapy. Its volume may vary in the course of febrile states. On palpation, its consistence is firm and rather elastic; the inferior pole is smooth. On four occasions, however, I have found a greatly enlarged spleen; in one case the clinical onset was splenic. Among the general phenomena, fever deserves a special place, even though it is not always present. Its type varies in different cases: recurrent (or intermittent with recurring bouts), continuous, or remittent with wide oscillations. The recurring type (50 per cent of cases) is characterized by an alternation of febrile periods (progressive increase, then progressive decrease) and of afebrile periods. A fever curve extending over a period of months gives a succession of parabolas. Frequently, the fever curve is less marked.

Deterioration of general condition in different degrees (anorexia, loss of weight and strength) often develops early* and characterizes the active phases of the disease; it may subside during spontaneous remissions.

Cutaneous Manifestations: Pruritus. This, the principal, disturbance often begins early, but it is far from constant. Pruritus, associated with other cardinal signs, constitutes a valuable differential point for clinical diagnosis; at the very first examination the patient should always be questioned on this point. Absence of pruritus, on the contrary, does not invalidate in any way the presumption of granulomatosis. Most often generalized (only the head being spared), the pruritus may be confined to a limited region (fixed or mobile). Sometimes it is so intense that it leaves the patient no respite, and we have seen it cause exhausting insomnias. The pruritus usually is not accompanied by granulomatous lesions of the skin and reflects a diffuse toxic action of the granulomatous virus and, as a rule, is not accompanied by scratch marks.

Other inconstant cutaneous manifestations include papular prurigo, exanthemata, lichenified lesions associated with scratching, etc. But sometimes cutaneous nodules or granulomatous tumors may attain the size of a bean or that of a walnut.

Hematology. The blood picture presents very inconstantly some interesting modifications. The number of erythrocytes is often abnormally low once the disease has become well established; in rare cases (toxic anemia), the number of these cells may fall very low. The percentage of hemoglobin follows a similar curve.

A moderate leukocytosis is the rule (the leukocytes numbering between 7,000 and 15,000); as extremes of leukopenia, and excluding the action of radiotherapy, the leukocytosis may reach 30,000, or even 90,000 cells (Guggenheim).

When modified, the leukocytic balance is more characteristic.

A polymorphonuclear leukocytosis, which should be carefully sought, is often observed (in 74 per cent of the cases, according to Aubertin and Levy). Eosinophilia is rather frequent, but is far from constant. When associated with polymorphonuclear leukocytosis, it becomes a valuable index. Eosinophilia in the blood does not parallel that of the lymphoid tissues removed for biopsy; usually the eosinophiles in the blood are not numerous, while the lymph nodes are rich in these cells (Chevallier).

* At the beginning of the disease, these general signs sometimes precede the appearance of other manifestations.

A very high eosinophilia of the blood (from 15 to 20 per cent upwards) would seem to go with the severe forms of the disease or to serve as an indication of the terminal phase.

From the diagnostic and prognostic points of view, Chevallier advises that, in patients with Hodgkin's disease, a combined polymorphonuclear and eosinophilic leukocytosis should be regarded as important.

Among the mononucleated cells, except for rare exceptions, the percentage of lymphocytes has diminished; when present, this lymphopenia is characteristic. On the other hand, a certain degree of monocytosis may be noted.

An increase in the platelets has been reported.

Abnormal nuclear forms are not found.

So much for the most common clinical symptoms.

Other clinical manifestations, rarely occurring at the outset, occur during periods of extension of the disease and reflect the tendency to general involvement.

In the first place, we may mention the lesions of bone which are especially common in the vertebrae and occasionally in the flat bones (pelvis, sternum, scapula), and also in the long bones (femur, tibia, etc.); sometimes silent, these lesions usually express themselves by spontaneous or induced pain which may be local or may radiate to remote parts, and sometimes by tumor formation; as soon as macroscopic lesions appear, they can be revealed by roentgenography. When left to themselves, they may end in collapse of the vertebrae (radicular compression, physiologic section of the cord), or in spontaneous fracture; most often, circumscribed foci form during an active phase of extension and may long remain stationary.

Roentgenographic study gives a good idea of most of these foci of bone involvement; it permits one to analyze their structure and to follow their evolution. The appearances of the vertebrae often reflect the mode of invasion: if this has proceeded from paravertebral masses of lymph nodes, the contours of the vertebral bodies, the articular processes, the lateral masses, the transverse processes or the costovertebral articulations are the first parts affected; when the mode of invasion resembles "infectious metastasis," the granulomatous process develops within the bone marrow, where it may cause alveolar formations or, on the contrary, may give to the bone an eburnated appearance. The intervertebral discs are always respected by the granulomatous process. The tendency to break down of the vertebral bodies is clearly less marked than it is in the case of neoplasms (Belot).

Bone involvement with multiple foci is less uncommon since the duration of the disease has been prolonged by radiotherapy, especially if a careful search for them is made.

Involvement of the central nervous system may be secondary either to mechanical accidents or to invasion of the cranial or spinal meninges (Askanazy), or again to infiltration of the nerve tissue itself; these are late complications which may be accompanied by mental confusion, jacksonian epilepsy, etc. Lesions in these situations bear a grave prognosis; we have observed them in 3 out of 77 cases.

Pleuropulmonary involvement is encountered with a certain frequency during the advanced stage of the disease; it may constitute a clinical type. Sometimes the lung alone may be invaded; in other cases the pleural phenomena dominate (effusion). Compression of a large bronchus by massed lymph nodes may cause atelectasis. Examination and roentgenologic inspection are valuable guides. Lesions of this kind make the prognosis even worse. Involvement of the larynx (arytenoids) is exceptional.

In one case we observed, late in the course of the disease, invasion of the pericardium with effusion. In another case, dysphagia was caused by extension of the disease to the esophagus (verified) from large masses of mediastinal nodes. Icterus from compression of the biliary channels

may occur as a rather late manifestation.

Primary involvement of the digestive tract, without demonstrable adenopathy, is rather rare: in such cases the disease affects especially the stomach and the upper part of the small intestine (Fränkel).

Finally, disturbances of the organs of special sense are very rare. Unilateral exophthalmos caused by invasion of the orbit has been observed.

CLINICAL PICTURE; EVOLUTIONARY ASPECTS

Malignant granuloma is characterized clinically by an extraordinary polymorphism. In relation to the variations in the initial site of adenopathy, to the varieties of extension, and to the successive syndromes which may dominate the evolution of the disease at different stages (especially in cases which have been modified by treatment), the greatest variety of clinical forms may be encountered. Even the age of the patient and certain physiologic states, such as pregnancy, may be factors. Finally, in addition to the foregoing, the many ways in which the disease evolves permit, by their character, a certain classification by the seal which they impress on the disease. The therapeutist should take this element into account in his estimations.

Without going into a detailed description, we may distinguish:

(*a*) The *lymphadenopathic forms*. According to the predominance of the affected regions and also according to the evolutionary stage, these are: peripheral region (a single adenopathic territory); a few or many peripheral regions involved; or again mediastinal, abdominal, paravertebral.

(*b*) Forms in which tissues outside the lymph nodes are predominantly affected (the adenopathic forms are rather rare). Splenic, pleural or pulmonary, osseous or osteoperiostic, nervous, cutaneous, gastrointestinal, or biliary, forms may be observed.

In the same patient, according to the dominant syndrome, and especially when the evolution of the disease has been modified by treatment, a transition from one form to another may be observed. Also, typical forms with all the major symptoms combined, or incomplete forms in which, for example, fever or pruritus, or splenic involvement, etc., are lacking, may be observed.

Like Chevallier and Bernard, we recognize four varieties of evolution, the limits of which are necessarily artificial: according to our statistics of 1934 (irradiated cases), they are as follows, in the order of their importance:

(*a*) Average forms, which are the most common (60 per cent of our cases), have an insidious onset. Adenopathy in some region develops and may remain confined to this region for a long time; or the clinical picture may suddenly change and one may observe the involvement of other groups of nodes; from the first the extension of the disease may affect both sides of the neck, both arm pits and both groins; the mediastinum is often invaded; deterioration of general condition is often accompanied by fever and itching. The disease proceeds by successive bursts, separated by spontaneous remissions or by remissions resulting from treatment, the former being usually inferior in quality to the latter. Then the disease becomes generalized and cachexia develops. From this time onward, accidents by compression of abdominal structures (edema, ascites, icterus), or of nerves may make their appearance. In some cases secondary infection may hasten the patient's death. When left to itself, the duration of this chronic progressive form is less than two years.

(*b*) Forms with slow evolution (20 per cent of our cases*) are relatively benign. They may progress slowly for years, even without active treatment of any kind; but they are also subject to sudden bursts of activity and may assume an acute character.

(*c*) The rapid forms may run their course

* By 1937 the proportion of this form had increased to 27 per cent (see influence of radiotherapy).

in a few months, and this onward progress is hardly modified by therapeutic efforts; the disease extends too rapidly; this form kills by its visceral lesions or by its complications rather than by pure cachexia (Chevallier).

Except for the terminal phase, the stages are the same as in the preceding forms, but they have an accelerated rhythm.

(*d*) Finally, acute forms are rare; their onset is brutal and accompanied by a high fever; from the very start, the general condition becomes greatly altered, and visceral manifestations are the rule. The disease runs its course in a few weeks.*

Later, we will consider in what measure the treatment is capable of modifying the types of evolution.

DIAGNOSIS

A thorough clinical examination, with thoracic roentgenoscopy and roentgenography according to the affected regions or tissues, and with hematologic examination, may lead to a strong presumption in favor of malignant granulomatosis if the syndrome is complete and if the evolution of the disease is characteristic, but it never can bring certainty. Moreover, the syndrome is often incomplete, especially at the beginning of the disease. Therefore, in the presence of a suspicious adenopathy (suppurative adenitis is a different story), a biopsy should be resorted to early, in order that a proper decision about treatment may be made, that the treatment may be instituted promptly, and that the application of roentgen therapy with reference to dosage and to the rhythm of irradiation may be rationally arranged. To make a false start would be to jeopardize the results of treatment in the majority of cases.

The results of histologic examination are not always conclusive: when this is the case, another node should be removed, not one just recently involved, nor one which has been involved a long time, and especially not an *irradiated node*.

But, in the last analysis, it is on the clinical features that the diagnosis really depends.

The disease must be differentiated from malignant tumors of lymph nodes, from myeloid leukemia, from aleukemic, tuberculous or syphilitic granulomas or lymphadenopathies, from tuberculous lymphadenitis, and from the subacute inguinal adenopathy of the disease of Nicolas and Favre. Clinical examination (with search for associated signs such as fever and pruritus), roentgenologic exploration, the examination of the blood, the biopsy, and eventually the biologic reactions, will almost always solve the problem. The radiotherapeutic test is admissible only in cases in which biopsy cannot well be done; for example, a mediastinal tumor without attendant adenopathy.

PART II

TREATMENT

Historical Summary (*up to 1920*). This incurable disease has been the object of numerous therapeutic attempts. Only the principal ones will be mentioned.

Surgical procedures have shown themselves useless; they do not influence the evolution of the disease. Local recurrence or extension develops shortly after operation except in the benign, local and peripheral forms, in which the lymph nodes are still movable.

Tonsillectomy followed by roentgen therapy, which was proposed by Holding and Brown, has fallen into oblivion. Serotherapy has not fulfilled its promises. Before the advent of roentgen rays, only *arsenical medication* (proposed by Billroth in 1871) has proved worth while. The results, however, have been very irregular and ephemeral, and the remissions obtained have usually been of mediocre quality. The average duration of the disease was not modified. As will appear later, this medication can retain a place as a therapeutic adjuvant.

* These last two groups include a certain number of atypical forms (with a "septicemic" gait, so to speak) in which the diagnosis is made only at necropsy.

Then came the *roentgenologic era:* Attempts to employ roentgen rays in Hodgkin's disease date back to 1902 and 1903 (Pusey, Williams, Senn); their observations were purely empirical, but were confirmed (1904–1905) by Bozzolo, by Levy-Dorn, and by Krause. The melting of the masses of enlarged nodes was impressive, but it was soon realized that the results were transient; the irradiated nodes soon recurred, and the evolution of the disease was not influenced.

At the same period, Heineke, who conducted experimental investigations (1903–1904), demonstrated histologically, in white mice and guinea pigs, the extreme sensitiveness to irradiation of healthy lymphoid tissues when subjected to the action of roentgen rays.

The facts discovered by Heineke were subsequently confirmed by all other investigators, and they explain the great sensitiveness of granulomatous lesions.

Roentgen therapy for malignant granulomatosis will slowly emerge from empiricism; patient efforts will be required if the combined progress of radiation biology and technique are to bear their fruits. In spite of excellent results by isolated workers (Hochgürtel, Schwarz, and others), one is hardly warranted in speaking of a rational roentgen therapy for malignant granulomatosis until after 1920. The reports and statistics published up to that time have shown interesting results, it is true; but because of unperfected apparatus, of inadequate methods of measurement, and of uncertain diagnosis, rational comparisons or conclusions cannot be made. With a few exceptions, that long period was characterized by the absence of lasting results (forms of the disease with long spontaneous remissions). Recurrence appeared at the very sites of the irradiated foci, often after very short intervals (a few weeks). The rays used were but slightly filtered and had little power of penetration. The small doses administered were given at long intervals (weekly, for instance) and were repeated over a long period of time. These technical conditions ended by sensitizing the integument (accidents) without exercising a deep, homogeneous, and lasting action, even on peripheral adenopathy. Therefore, what could be expected from irradiation of mediastinal or other deeply situated nodes? Most often the failures multiplied, the patients being abandoned to their fate. Only because of the ineffectiveness of any other treatment did roentgen therapy maintain a mediocre credit.

Between 1918 and 1920, the schools of Freiburg in Breisgau and of Erlangen reported the results obtained with more penetrating roentgen therapy, with a more selective (heavy filters) quality of radiation. The authors stressed particularly the very different biologic value of a *given dose* according to whether it was administered in a single session or, for example, in ten separate sessions on successive days (fractional irradiation). The application of a massive dose in one session, corresponding to a certain type of cutaneous erythema (H.E.D.) was advocated not only for cancer but even for simple ovarian castration. Malignant granulomatosis did not escape the new vogue, but the results were disastrous. The local effect was distinctly superior, but the abrupt and massive absorption of albuminoids often caused serious general accidents. These were not always a mere result of intoxication; in one case with mediastinal involvement reported by Czepa the sudden appearance of edema (early reaction) caused the death of the patient in a few hours.

Nevertheless, the excellent publications of Krönig and Friedrich, and of Seitz and Wintz, marked a turning point in the history of roentgen therapy and opened new perspectives to investigators.

In dosage the problem of the time factor assumed fresh importance, and the treatment of malignant granulomatosis soon felt the benefit of its application.

Mode of Action of Roentgen Therapy in Malignant Granulomatosis. Radiosensitiveness. The clinical observations of Pusey, of Williams, and of Senn showed the exquisite

radiosensitiveness of granulomatous tissues; the experiments of Heineke explained it and justified recourse to roentgen therapy. As for the study of irradiated Hodgkin's tissue, this dates back only about ten years. Between times, the hypothesis of an indirect dominant action was advanced by some authors.

1. How does the granulomatous lymph node behave when subjected to so-called segmental or local* irradiation?

Clinically, it melts in a few days, and the duration of this regression corresponds to the time necessary for the destruction and disappearance of the lymphoid cells. The node may disappear completely or may leave a sclerosed residue which may still be palpable.

The disappearance of the node may be permanent, especially with the present techniques; thenceforth the node no longer participates in the subsequent extension of the disease. In other cases the node, after remaining silent a long time, again increases in size; this is local recurrence.

To what histologic aspects do these modifications correspond?

The microscopic inspection of irradiated nodes shows that, during the hyperplastic and granulomatous stages, the main action of the rays is destructive or cytolytic; large foci of necrosis appear. Of the different cells of the granuloma, which are unequally radiosensitive, the lymphocytes and other undifferentiated cells are the first to disappear; then, in turn, the polymorphonuclears and finally the Sternberg cells disappear; these last are pycnotic. Mitotic figures, which were very numerous before irradiation, become extremely rare.

The necroses produced by roentgen therapy are followed by a fibro-constructive process (analogous to that which we have already described (Part 1)), with this difference that the induced cellular destruction gives rise to a more energetic reaction of the organism—a reaction which may end in complete cicatrization. Thenceforth, either the sterilization of the cells is complete (solid or "cicatricial" sclerosis) or the fibrosis is only partial. Within the zone of fibrosis a more or less important lymphoid residue persists (perhaps because of insufficient irradiation†), which is still virulent or capable of becoming so. This means recurrence *in situ* after a short or a long interval.

Broadly, such are the results of the comparative studies of lymph nodes removed before and after segmental irradiation (Laignel-Lavastine and Coulaud, Schiffner, Askanazy, Babaïantz, Chevallier and Bernard, and others). Recently, Brunschwig and Kaudel, who studied the histologic changes in relation to the clinical observations, observed in one irradiated case a complete sclerosis of the granulomatous nodes; they think that roentgen therapy can be successful only in early cases when subjected to sufficiently intense doses. As for the normal nodes, they do not undergo sclerosis; islands of mother cells persist, and from these regeneration occurs. Histologic examination of recurring nodes shows nothing more than a cellular repopulation similar to that which I have just described, beginning from pathologic islands which may often be seen in incompletely sclerosed nodes.

2. *Behavior of Granulomatous Foci Outside the Lymph Nodes.* We have seen that, besides the lymph nodes themselves, most of the tissues and organs may be invaded. As for the action of roentgen therapy on the histologic evolution of granulomatous foci in internal organs, satisfactory information is lacking because of the difficulty of obtaining tissue at different stages of treatment. Roentgenographic data are very insufficient to fill this gap. We may suppose that these granulomatous infiltrates are destroyed or modified in a manner which does not differ essentially from

* These terms distinguish ordinary roentgen therapy from total teleroentgen therapy.

† The persistence of granulomatous foci may also be observed in cases in which the treatment has been properly given. "The more a disease tends to evolve, the more the patient continues to have fever, the smaller the chance of finding an intense sclerosis" (Chevallier and Bernard).

the manner in which the rays act on the lymph nodes.

The *osseous foci*, in which roentgen therapy often yields durable results, have been studied more carefully. In many cases one may observe and follow the regeneration of the irradiated bone which may recover its normal appearance (Friedrich), but most often an evolution toward a hyperplastic appearance is observed (Caillau, Belot, Dresser, Gilbert). In other cases the bony lacunae, which Askanazy has compared to foci of dry caries, persist after roentgen therapy but do not undergo further evolution; roentgenography enables one to follow them from time to time during the course of remarkable remissions (for example, Case 14, Table VII). The cases in which it has been possible to obtain serial biopsies of bone are rather rare; these demonstrate the destruction of the granulomatous cells and the regeneration often revealed by roentgenography. In the central zone of a vertebral body, for instance, microscopic examination shows the organization of a chancroid tissue, and in the periosteum the elaboration of a compact, dense and prominent bone marrow which is richer in calcium salts (Caillau). Exceptionally, the osteoplastic reaction appears also in the nonirradiated bone (Chevallier); on the contrary, it represents the usual response of bone tissue to roentgen therapy (Case 51, Figs. 6, 7 and 8).

Necropsies on Lymphogranulomatous Patients. With reference to the lungs, necropsy of one of Czepa's cases enabled him to prove an early edema provoked by excessive irradiation. In cases of intensive irradiation, Evans and Leucutia found an edematous infiltration of the pulmonary parenchyma and a proliferation of perivascular and peribronchial fibrous connective tissue ending in a destruction of pulmonary architecture. In 1 of my 77 cases (Case 16), death followed anoxemia five years after the beginning of roentgen therapy; the necropsy (Askanazy) demonstrated a "bilateral pulmonary sclerosis with chronic desquamative pneumonia"; besides this the protocol mentions "sclerosis of the entire lymphoid apparatus with almost complete disappearance of lymphoid tissue from the lymph nodes and from the spleen; hyperplasia of the islands of Langerhans (old lymphogranulomatosis which cannot be recognized)." In 2 other previously biopsied cases, as in the last case, in which the patients died of an intercurrent disease many years after roentgen therapy (Cases 31 and 39), it was impossible to find, at necropsy, any trace of granulomatous tissue in the old foci. Schwarz and Fleischner have made similar observations.

In segmental roentgen therapy, the rays have a direct, elective action on the granulomatous lesion by destroying the cells of which it is composed. This, at least, is the main action observed and on which we must depend. If there is any indirect action, especially an action involving the sympathetic nervous system, this is hard to prove and would appear to be a mere accessory.

In teleroentgen therapy the question seems to assume a different aspect. The biologic effects are much more complex, but we do not yet possess sufficient information to understand them, at least as they relate to Hodgkin's disease. This will be the task of tomorrow.

RADIOSENSITIVENESS

3. Does histologic examination of granulomatous lymph nodes (biopsy) furnish indications on the *radiosensitiveness* of the case in question?

We have seen that the granulomatous node passes through a cellular stage and finally ends in a fibrous stage. If a biopsy reveals a form with strong cellular predominance and numerous mitoses, and if the clinical picture on the whole is in harmony (young, rapidly growing tumors), we may assume, especially during the first phase of the disease, a good degree of radiosensitiveness. If, on the contrary, the biopsy should reveal a lymphoid structure very poor in cells but rich in connective tissue, and if the nodes are clinically small and hard, we may fear a certain degree of

radioresistance. I have made this contrasting observation in 2 cases which were subjected to biopsy, then irradiated, and which were observed at the same time in 1922. The latter form is rather exceptional.

Besides these extreme cases, considered both histologically and clinically before any treatment, microscopic examination does not furnish any more indication concerning radiosensitiveness than it does in cases of recurrence. The question of radiosensitiveness remains obscure. Schwarz (1935) compared 2 cases of mediastinal tumor: the one responded to 600 r, at a depth, given in fifteen days; while the other required 2,100 r, at a depth, in two successive series. Aubertin and Destouches recorded a case in which certain groups of lymph nodes proved very radiosensitive, while others from the very beginning showed themselves very resistant to treatment. Gilbert and Babaïantz noted the coexistence of all the histologic stages in the same group of lymph nodes removed for biopsy, before any irradiation. Does the histologic make-up of the granulomatous foci play a rôle in the differences in radiosensitiveness which are observed clinically? This is possible, but I cannot go any farther.

4. As for the radioresistance acquired by repeated roentgen therapy, to which many authors have drawn attention, no underlying anatomic basis for it is known. However, I have observed it only during the terminal phase of the disease or in patients who had previously been subjected to small doses at long intervals and repeated for a long time. Moreover, it was on the strength of this clinical observation that, as early as 1922, I abandoned this method of irradiation and adopted a method which, as concerns the administration of the dose, is based on principles admitted as sound in the treatment of malignant tumors. Some recent investigations by Ferroux, Regaud and Samssonow (1937) seem to bring to this clinical observation an experimental proof of great interest. Their study, bearing on seminal epithelium, proves the increase in radioresistance of this tissue under the influence of small doses (repeated at intervals) of roentgen rays. Certain bad therapeutic methods which are of this kind are not rare in Hodgkin's disease; by analogy, therefore, it is permissible to think that the increasing radioresistance of irradiated cases of granuloma may have such an origin.

Summarizing, segmental roentgen therapy exercises a direct destructive effect (cytolysis) on granulomatous tissues. Whatever may be the site of the lymphoid or extralymphoid focus, the mechanism of destruction and of fibrous connective tissue reconstitution appears to be the same everywhere, if we allow for differences in environment (Gilbert and Sluys). The fibrous connective tissue process is but an increase in the spontaneous process of fibrosis which is observed without reference to roentgen therapy.

When local recurrences take place they begin in residual granulomatous islands often left, during the first stage of the disease, after inadequate irradiation.

As a rule, histologic study does not furnish any indication as to the radiosensitiveness of granulomatous tissues.

The question of radioresistance acquired by repeated roentgen therapy is entirely different. This is a general phenomenon which is still obscure and difficult to interpret. This acquired resistance interferes little with roentgen therapy for malignant granuloma if the radiologist endeavors to obtain as complete as possible a destruction of the pathologic foci at the very first course of treatment, and if he avoids further irradiation in the absence of recurrence. On the contrary, it has many chances of appearing early and of jeopardizing the results of treatment if the patient is first exposed repeatedly at intervals to small doses of rays of short wave length.

SELECTION OF THE METHOD OF TREATMENT—TECHNICAL MODALITIES

The clinical application of roentgen therapy requires first a correct solution of the technical problem. To avoid any misunderstanding, I shall add that the efficacy of the

treatment depends largely on our knowledge of radiobiology and on our clinical sense. The treatment cannot be standardized; in malignant granuloma especially, the treatment must be adapted to the individual patient, and in each case it must be adapted to the different stages of the disease.

Object of Treatment. The object is to obtain as frank and as long remissions as possible, and to give the patient, with an illusion of recovered health, full capacity to work.

This implies the destruction of all the granulomatous foci, deep and superficial, without jeopardizing the general condition of the patient or the condition of the blood.

Choice between Roentgen Therapy and Radium Therapy. The destruction of the granulomatous foci requires not only a good percentage depth transmission of the rays but also the irradiation of large areas or volumes of tissue.

At the time when only rays of medium penetration were available, many radiologists turned to radium. Whereas in America *packs* were preferred, in Europe *moulded applicators* were employed for therapy from the surface. The highly filtered tubes containing the radiant energy were placed at a certain distance from the skin in order to obtain a satisfactory space distribution and to attenuate the disadvantage of too rapid a decrease of intensity within the irradiated tissues. The methods of radium therapy exerted their effect with great gentleness on the peripheral granulomatous foci (weak hourly intensity, continuous irradiation over a prolonged period); but, except where large quantities of radium were available, the deeply situated pathologic foci received an insufficient quantity of energy because of the short distance between the radioactive tubes and the skin; and thus it was difficult to irradiate sufficiently large surfaces.

Nevertheless, radium therapy, alone or combined with roentgen therapy, yielded excellent results in Hodgkin's disease, as may be seen from the published reports of Bowing, Desjardins, Schreiner and Mattick, Dautwitz, Burnam, and others. Pinch and Levin used this method only for peripheral adenopathies. Lazarus attacked mediastinal tumors by combining external irradiation with irradiation derived from tubes of radium or mesothorium introduced into the esophagus.

Then, as the result of advances in penetrating roentgen therapy, radium treatment for Hodgkin's disease was relegated to second place, except for a few institutes richly endowed with radium.

This evolution was the more comprehensible since we have no proof that roentgen rays have a different biologic action than the gamma rays of radium. Schreiner and Mattick, who reported 46 cases of malignant granuloma treated with roentgen rays or with radium (1924), did not observe any difference in the mode of action. Holthusen maintains that a radiosensitive form of lymphogranulomatosis responds as well to roentgen therapy as to radium therapy.

The radioactive substances, however, have certain indications. Thus Mallet employs surface radium treatment for patients who cannot be moved, by moving the radioactive source from one point to another in relation to the invaded regions. But recourse to radium or to thorium X has been advocated especially in cases of radioresistance arising after roentgen treatment (Desjardins, Dautwitz, Mallet and Cottenot, Coliez, Schwarz, and others). For my part, although I follow most of my granulomatous patients until the final stage, I have not had to employ this procedure; on the contrary, I have successfully used penetrating roentgen therapy for patients who had been incorrectly treated with inadequate doses, either by long repeated, fractional irradiation, or by repeated exposure at intervals to too soft, slightly filtered roentgen rays (certain patients, who presented early recurrence *in situ*, also gave undeniable evidence of it). As would have followed the use of radium, the use of sufficient doses of well selected, penetrating roentgen rays has enabled me

to obtain often important, and sometimes renewable, remissions. Of course, I do not deny that granulomatous patients may not acquire, after repeated series of irradiations, a certain degree of radioresistance; but, from my observations, the great majority of cases treated early with effective deep doses of roentgen rays do not show radioresistance except at an advanced stage of the disease. It is doubtful if, during this phase of generalization and cachexia, radium treatment can still exert an appreciable action.

Until now, teleradium therapy does not appear to have been employed in Hodgkin's disease. On the other hand, mention should be made of *alpha therapy* which, according to the radioactive substance injected, has been carried to the muscles, to the tumor or to the veins, and has yielded very unequal palliative results. Aubertin, as well as Billich, has noted favorable effects from thorium X, while Stevens (radium chloride), Laborde and Nemours (thorium X and mesothorium), had some complete failures, and even saw the disease aggravated. In exceptional cases I have injected radon intravenously (Wassmer syringe) to complement roentgen therapy during the last stage. In a general way, the injection method is a blind procedure; in the case of intravenous injections, the small quantity of substance scatters in the organism and is eliminated through the respiratory and other natural channels. At most, one may expect from it an adjuvant effect, provided one avoids local accidents due to the caustic action of the alpha rays. From the combination of thorium with roentgen therapy Falta and Schwarz have obtained similar results in cases which had become radioresistant.

Summing up, in choosing between roentgen therapy and gamma-ray therapy, considerations of technique and clinical application, and not biologic factors, should be our main guides. Except in special cases, therefore, it is logical to give the preference to roentgen therapy. This is the opinion of the majority of therapeutic radiologists.

Quality of the Rays: Penetrating or Semipenetrating Roentgen Therapy. If roentgen therapy is the method of choice, it should be specified that we refer only to roentgen therapy of sufficient penetration to enable one to administer at the level of the deepest foci of disease quantities of energy capable of sterilizing all the pathologic foci. Moreover, deep roentgen therapy has the inestimable advantage, in a recurring disease which requires several series of treatments, of being repeated for a long time without risk of cutaneous accidents, provided suitable doses are given in proper order. Today the great majority of radiologists agree on these points. By sufficiently penetrating roentgen therapy I mean roentgen therapy between 170 and 200 kv., a filtration of at least 0.5 mm. of copper (corresponding to a half-value layer of about 0.9 mm. of copper), focal distances varying between 35 and 60 cm., on the average, according to the seat and volume of the masses to be irradiated.

As early as 1922, I was led to adopt penetrating roentgen therapy by having previously had failures in 4 successive cases (early peripheral recurrences *in situ*) as the result of using rays of slight penetrating power, filtered through 2 or 3 mm. Al (the dose on the skin varying between 5 and 10 H, given once a week for many consecutive weeks). For this disease, evidently, these conditions of irradiation were mediocre.

Moderately penetrating roentgen therapy has had its partisans: a nong these, Desjardins (1927) preferred to use, at the beginning of the treatment, a potential of 140 kv., the better to overcome later, by means of roentgen therapy at 200 kv., lymphogranulomas which had become radioresistant. On this basis, O'Brien (1936) employed, for successive series, treatment at 165, 185 then 200 kv. (in 1936 he seems to have adopted penetrating roentgen therapy). We have seen how, in the same order of ideas, radium was recommended. In my opinion, this advantage may be preserved if we use, for the first series of

irradiation, doses that are not too high but with technical factors which insure the most effective depth dose. Thus is preserved the possibility of increasing later the surface dose, the penetration, or both at the same time, in order to augment the dose received by the pathologic foci. Perhaps the advances of the last few years (high potentials) may render this task still more easy.

One last word on the quality of the rays. I do not hesitate to call a professional error the application of unfiltered or barely filtered rays to granulomatous adenopathies. Even an error in diagnosis does not justify them. These patients come to the radiologist seeking treatment for early recurrences *in situ*, when the skin still bears the marks of an abnormal accumulation of radiant energy, if not even more. Such reactions are no longer seen, even after repeated treatment, since we have employed sufficiently selective and penetrating rays.

Dosage—Rôle of the Time Factor (*Rhythm of Irradiation*). The criterion of good roentgen therapy (due consideration being given to the evolutionary types of the disease) is a prolonged remission which, in the average chronic forms, may often extend from one to two years after the first treatment. In this connection, the importance of the question of dosage and of the rhythm of irradiation must receive full attention.

The most desirable dose should be the smallest total dose capable of destroying all the granulomatous tissue without jeopardizing the patient's general condition or the condition of his blood.

Experience has condemned small doses given at intervals (weekly, for example), repeated for a long time, directed only to the most apparent manifestations, and without a general plan. It has also condemned massive doses given at one sitting. Since 1920, it has pointed toward fractional doses, given at short intervals and with a total dose sufficient to maintain their activity. This idea of strong but fractional doses has gradually won over almost all therapeutic radiologists.

As developed since 1920, doses may be broken into fractions in many different ways. Before going into this subject, I wish to render homage to the perspicacity of G. Schwarz, a master of the Viennese school who, as early as 1914, advised in connection with a granulomatous tumor of the mediastinum—I discovered this while preparing this report—"not to apply at long intervals full doses at one time, but to use a method of treatment extended in time ('Dauerbestrahlung'), which consists in giving daily relatively small but still active doses." Born of experience and clinical observation, this wise advice did not receive the attention it deserved.

While Schreiner and Mattick (1924) gave a depth dose of 60 to 70 per cent of the "human erythema dose" in two or three consecutive days ("treatment of attack"), Holthusen (1926) advocated 60 to 70 per cent H.E.D. ("Herddosis") but to allow a rest period of two or three days between sessions; the incident dose is 30 to 50 per cent H.E.D. Voorhoeve (1925) recommended a depth dose of 70 per cent H.E.D.; he spread the treatment over two or three weeks, with a total dose per field of 90 per cent H.E.D. and often gave a second series after an interval of three months. Gilbert (1923) originally advised a minimal depth dose of 50 per cent of the H.E.D. of Wintz (given for one field in two or three days); then, alternating the fields, he increased the total dose but spread it over ten to fifteen days for each field so as to obtain a depth dose of at least 500 r for the first series of irradiations (radiosensitive forms), the series altogether not exceeding a total of five weeks (daily sessions);* the dose at each session does not exceed 250 r on the skin (about 180 r in air for a field 150 cm.²); at the beginning in the case of massive adenopathy, the dose is only half as much; in the forms in which the clinical response is slower, the doses should be increased. Schwarz (1935), who observed wide variations in radio-

* Technique mentioned in 1925, given in detail in 1928 and in 1931 by Babaïantz.

sensitiveness, does not specify the total dose, but only the depth dose at each session: 50 to 80 r, at most 100 r; he irradiates at a focal distance of 60 cm.; the doses at each session do not exceed 250 r on the skin; his fields may be as large as 800 cm.^{2}; his guide is the regression of the clinical manifestations. In a case of mediastinal tumor, a depth dose of 700 r given in two weeks yields successful results, while in another case the same dose must be followed by a second series (1,400 r in six weeks) in order to obtain a corresponding disappearance of the tumor. This fact, which is not exceptional, is full of instruction.

The idea of a treatment of attack—that is, of energetic doses at the beginning of irradiation—is found here and there in published communications; certain authors also advocate treatments of maintenance or prophylactic treatments (Aubertin and Thoyer-Rozat, and others); I shall consider this again later. Just as we do, many authors insist on the necessity of adapting the treatment to each case, aside from any general plan.

In 1923, Chaoul and Lange proposed a special method based on 12 cases and on excellent results for that period. As a reaction against massive doses, they employed fractional irradiation with the fractions more scattered in time and with much smaller doses at each session. But while, until then, it had been only a question of relatively local irradiation, Chaoul divided the trunk of the patient (including the neck and groins) into four large fields, two dorsal and two ventral, to which he gave, daily at first but later with increasing intervals (1, 2, 3 and 7 days), 10 per cent H.E.D. up to a total dose of 60 to 80 per cent H.E.D. per field; the course of treatment, therefore, was spread over six to eight weeks; moreover, irradiation was repeated after an interval of three months, and again after one year. This study appears to be a first step toward the methods of total irradiation which will be discussed later. In connection with their dosage I shall say a few words now.

Total teleroentgen therapy (Teschendorf, 1927) requires, on the part of the therapeutic radiologist, extreme prudence; especially in cases of lymphogranulomatosis, Sluys (1931–1933) has shown that the threshold of dosage which does not produce serious disturbances is very low; he advises beginning with a dose varying between 10 and 30 r, in order to test the sensitiveness of the patient. A dose of 30 r usually causes vomiting, agitation, insomnia and fever; the treatment should be stopped. If, on the contrary, this is undertaken prudently, if one remains within the threshold dose of toxicity (in certain cases the dose may be increased up to 50 r a day), excellent results may be obtained; the symptoms abate, the patient regains weight and may be able to resume work which he had had to give up. Marchal and Mallet (1933), and also Cottenot and Lemoine (1934), write in the same vein; they estimate that, besides the question of dosage, there exists a very complex set of biologic factors which together constitute individual tolerance; if they sometimes note inadequate results, exhaustion of the effects of irradiation, such a scheme of treatment would, during the course of a remission, permit the organism to become sensitive again to local irradiations, and vice versa in the case of acquired radioresistance. Later, we will again consider their results which are rather recent.

One method which rather resembles that of Chaoul and Lange was proposed between times (1930) by Sluys for the treatment of malignant granulomatosis under the name of *total roentgenization through large separate fields*. This method consists in dividing the entire cutaneous surface of the patient into about ten to fourteen fields (five to seven anterior fields and five to seven posterior fields). On the first day Sluys gives a dose of 500 R (Solomon) to one field (or 250 R to each of two fields). If this first dose is well tolerated—which is usually the case—he gives 500 R each day or every second day until each field has been irradiated four times.

Local, segmental roentgen therapy? or

total roentgen therapy? During the last few years, this point has undoubtedly caused more controversies than any other since Teschendorf (1927) advocated total teleroentgen therapy, not only in diseases of the blood but primarily in malignant granulomatosis.

If we interpret them literally, the two terms which I use here represent two extreme conceptions. In fact, in a systemic disease such as this, the discussion (prior to teleroentgen therapy) first bore on the greater or smaller extent of segmental roentgen therapy. I shall not take time now to discuss the old fashioned idea of irradiating, through limited fields barely large enough to include visible groups of enlarged nodes, patients with lymphogranulomatosis, as one would irradiate a tuberculous adenitis; this procedure, which usually ends in failure, recalls by its results the era of surgical treatment.

(1) In segmental roentgen therapy, three conceptions have gained adherents:

A. To irradiate only the clinical manifestations, and to avoid with care parts of the lymphatic system which appear to be healthy (Voorhoeve, Kruchen).*

B. Wide irradiation of the regions patently invaded, as well as regions suspected of invasion (Bowing, Desjardins, Gilbert, Schwarz, and others).

C. To irradiate the entire trunk, including the cervical and inguinal regions (Chaoul and Lange). The method of roentgen irradiation proposed by Sluys differs only slightly from C.

For lack of a precise criterion which would permit us to choose between these three conceptions, we will allow ourselves to be guided by our anatomic and clinical knowledge and by clinical observation.

Many times I have seen, in patients recently treated for peripheral adenopathy, recurrence developing in the immediate vicinity of a field too narrowly irradiated (A). On the contrary, I do not recall having observed such recurrence in patients to whom I had methodically applied the principles enunciated under B. By this means, without doubt, healthy portions of lymphoid tissue are often irradiated, but still more often we include in one large field portions already invaded, if only histologically, and it is this which we must seek because, as Beaujard (1928) has observed, the question is not to protect prophylactically groups of normal lymph nodes against future invasion.

The difficulty is to know how far one must irradiate. If one is dealing with a form of the disease which is still confined to certain regions, for example, unilateral cervico-axillary and mediastinal, symmetrical irradiation of these regions is indicated. If the general signs improve during the treatment, while the tumors melt, we may abstain from irradiating other parts of the trunk provided the patient is kept under observation.† If, on the contrary, the general signs persist (fever, pruritus, asthenia, etc.), irradiation should be extended to the paravertebral regions (Desjardins), to the retroperitoneal and para-aortic nodes, and eventually to the spleen. If, from the beginning, the disease involves many regions, we must direct our attack widely toward the demonstrable manifestations until they are eliminated; then, as far as the general condition and that of the blood permit, toward the entire abdominal cavity (eventually in a complementary series, after a rest of at least six weeks, general tonics, arsenical and ferruginous medication, or even transfusion, in order again to be able to use active doses). In spite of this, failure is frequent.

This method of procedure (B) is infinitely surer than that mentioned under A and, during the fifteen years I have followed it, I have never observed any disadvantage.

As for the conception of Chaoul and Lange (C) its use when the disease is generalized may be defended, but because

* To judge by the dimensions of the field (up to 150 square cm.), it would seem that Holfelder accepts this conception.

† During the early years this shade of distinction was not made.

of the spacing in time and the small doses absorbed, and because of the automatic repetition of the series of irradiations, I doubt if in many cases it can yield long term results;* it can succeed only in very radiosensitive, generalized forms of the disease, in which small doses are sufficient; in other cases, it doubtless will not prove more successful than B. If, on the contrary, one has to deal with a regional form, the method of irradiating the entire trunk exceeds its object: the many favorable results obtained by more restricted irradiation provide ample testimony on this point.

In conclusion, I do not hesitate to give preference to the conception enounced under B; it has given me entire satisfaction. The determination of the size of the fields, which varies from one patient to another, and in the same patient at different stages of the disease, cannot be specified;† above all, this is a question of clinical flair and restraint; on the one hand, it is essential to irradiate widely enough to be reasonably certain to subject to the action of the rays the entire invaded region; on the other hand, one must constantly strive to save the general condition of the patient and to safeguard his means of defense. Thus we follow sound clinical practice in roentgen therapy.

(2) *Total roentgen therapy* in malignant granulomatosis should be eliminated forthwith, after the comments which we have just made. However, the biologic problem raised by teleroentgen therapy is at once new and delicate. The mode of action appears complex. Thus, the cellulicidal action, which is the most important in segmental roentgen therapy with the doses considered, becomes less important in teleroentgen therapy and, according to the hypothesis of Desplats, apparently leaves more space for an indirect, humoral or functional action. Moreover, when one considers the doses used (10 to 30 r a session), the spacing of the sessions in time, and the total doses, it is difficult to conceive a direct destructive action on the granulomatous tissues. Perhaps experiments will help to unravel the skein; the best we can do at the moment is to analyze the clinical results of panteleroentgen therapy.

These results are still far from numerous. After nine years of experience, Teschendorf (1924) advised against the method in malignant granulomatosis, while preferring it in the leukemias. Basing his opinions on those of Teschendorf and on his own observations, Schwarz (1935) as well as Holfelder opposed total teleroentgen therapy for Hodgkin's disease. Belot (1935) expressed strong doubt that the small doses absorbed at the level of the granulomatous foci can suffice to destroy the tissues in question; experience has taught him that, to obtain a favorable result, the sessions of treatment must be repeated and, in most cases, the total dose must be sufficient to jeopardize the general condition and the blood formula. On irradiating large mediastinal tumors, Ponthus and Piante noted an improvement in general condition but a mediocre local effect; but on subjecting the mediastinum to classic segmental roentgen therapy, they saw the tumors melt. On the contrary, Marchal, Mallet, Cottenot and Lemoine (1934), who irradiated cases of leukemia and of Hodgkin's disease, declared that their earlier optimism in leukemia had diminished, while their results in granulomatosis were distinctly better than in 1933. Let us look a little more closely; of 18 patients with Hodgkin's disease treated during different phases of the disease, they reported excellent results in half of the cases, and 9 patients were in a state of apparent cure; but of these 9 patients only 5 had been treated with total teleroentgen therapy alone; the others had also received local roentgen therapy, but this falls within the conception of the authors. Under these circumstances (small number of cases, short period of observation, dangers of the method), these results can be accepted

* I am not aware of any publication on this subject by Chaoul since 1923.

† Later on, nevertheless, we give an outline, but only for general orientation.

only with great reserve; any comparison with the results of segmental roentgen therapy, which has proved its efficacy, is still impossible.

We may conclude that, at the present time, local, segmental roentgen therapy clearly surpasses panteleroentgen therapy in advantages and in safety. With this last method the regression of enlarged lymph nodes is less pronounced and less durable, while the general reactions and especially

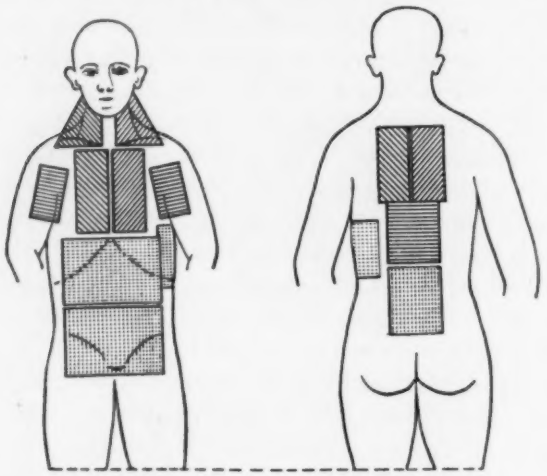


FIG. 1. Plan of irradiation for a cervical and mediastinal form with suspicion of mediastinal involvement. (In full lines are drawn the fields to be thoroughly irradiated from the first—From Gilbert and Babaïantz.)

the risk of accidents are distinctly greater. The future will show if this view will have to be modified.

Repetition of Roentgen Therapy. Repetition of roentgen therapy is indicated only *in the event of recurrence*—except in special cases in which a tumor mass has not undergone sufficient regression.

If the object of the first series of irradiations—destruction of the granulomatous foci—has been clinically attained, there is no reason to use a "maintenance treatment" or "prophylactic irradiations"; these can exercise a useful action only in the presence of active granulomatous foci; under these conditions, I feel that the economy of dosage, as well as the respect due to the integument, impose abstention. I have not diverged from this course since 1922, and the patients have been the better for it.

I know that my views on this point are not shared by many authors; I hope to convince them by the facts herein recorded.

The principle of abstention has for corollary a careful observation of treated patients, for years if necessary, in order to discover recurrences early and to combat them without delay.

In this connection it should be mentioned that the discovery of recurrences is not always easy; thus the cases in which a local enlargement of lymph nodes cannot be disclosed while general manifestations (fever, pruritus, asthenia) or even blood manifestations (for example, leukocytosis, neutrophilic polymorphonucleosis) alone betray an offensive return of the disease. In such cases one must attempt to irradiate practically the entire abdominal cavity; if improvement follows, one should persevere while taking into account the general and blood reactions; if improvement does not occur, two contingencies may take place: either the patient is too ill and roentgen therapy should be given up in favor of symptomatic medical treatment; or, if the general condition is relatively good, one should try with great care and with frequent examination of the blood panteleroentgen therapy, and later total irradiation through large separate fields, as advocated by Sluys. For my part, I do not believe in the efficacy of these methods under such circumstances.

For the purpose of orientation, here are the principal elements of the method which I published with Babaïantz some time ago:

1. The diagnosis having been made (biopsy), to determine, after a thorough examination, with the aid of roentgen diagnosis, all the clinically discoverable foci.

2. Segmental roentgen therapy.* To establish a plan of irradiation: to aim first to irradiate widely the regions clinically in-

* In principle, malignant granulomatosis should not be subjected to total teleroentgen therapy.

vaded; then, if it should be necessary (persistence of general signs such as fever, pruritus, etc.), irradiation of suspected regions.

The order of irradiation varies with the clinical forms and the regions involved (for the purpose of orientation only, we give a plan of the fields which most often have to be irradiated—sometimes in two stages, at intervals of six weeks: see Fig. 1).

3. Technique of penetrating irradiation: 180 to 200 kv.; filtration of 0.5 to 1 mm. of copper+1 mm. of aluminum; half-layer value of 0.95 to 1.65 mm. of copper according to the filtration and apparatus; variable focal distances (35 to 60 cm.) according to the depth of the lesion and the dimensions of the field (these may sometimes increase to 400 sq. cm.) (Fig. 1).

4. Simple, daily, fractional irradiations, directed successively toward each invaded region or, in certain cases, directed toward the regions of greatest involvement. Thanks to the rotating plan, each field is irradiated only at intervals of about two days *until an adequate total dose has been given.*

Incident dose at each session: up to 250 r —effective dose on the skin—(or 180 r in air for a field 150 sq. cm.). Much less at the beginning, if the patient's general condition is bad or if the lymph nodes are very large. The number of r per minute (10 to 20) should be reduced (Coutard type) only in cases requiring special care of the general tissues.

Total incident dose. Until now we have specified an order of magnitude; but, with the present variations (chiefly in focal distance), one should preferably be guided by the transmission values and by clinical observation; we usually irradiate cervical, axillary, and other adenopathies through a single field; mediastinal tumors through two or more fields with converging beams.

The minimal total depth dose to be attained for each focus is 500 r in very radiosensitive forms early in the disease; it should be increased under clinical control in the less sensitive forms, due consideration being given to the general condition, the condition of the blood, and the tolerance of the irradiated tissues (a new series after an interval of six weeks if a large tumor has not regressed sufficiently).

Duration of treatment. The foregoing specifications apply when the treatment of each field covers ten to fifteen days, and when the total duration of treatment is about five weeks; although they are not rigid, especially if the pathologic process is very extensive, it would be well to adhere to them as much as possible.

A double danger should be avoided: too small total doses would partially destroy the granulomatous foci and the patient would be exposed to early recurrence *in situ;* too large doses would exceed the requirements, would risk jeopardizing the subsequent efficacy of roentgen therapy in the event of recurrence, or would force a premature interruption of irradiation on account of leukopenia and general reactions.

5. *Adjuvant treatment.*

In the majority of cases the treatment may be ambulatory if the patients live in the same town or nearby.

6. *Repetition of roentgen therapy:* only on the appearance of recurrence. However, treated patients should be kept under periodic and careful observation.

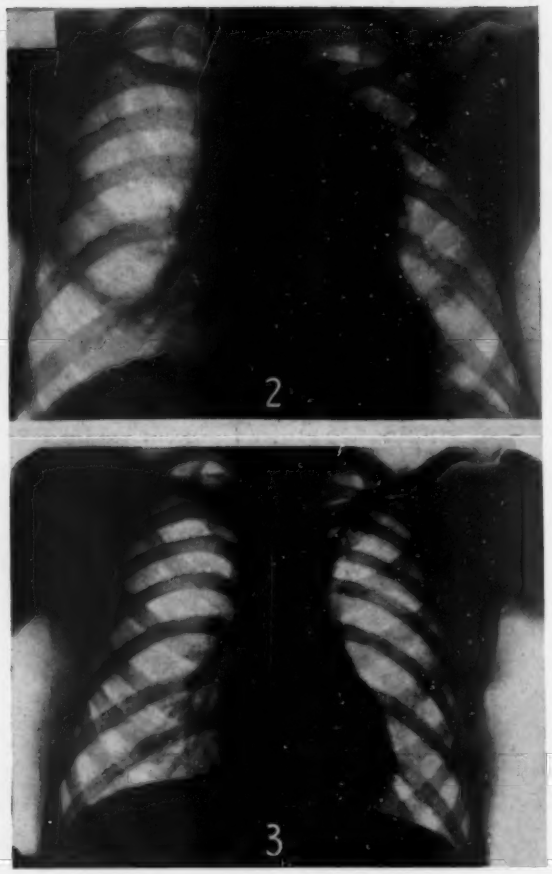
RESULTS OF ROENTGEN THERAPY

A. CLINICAL ASPECTS

1. *Influence of Roentgen Therapy on the Principal Symptoms.*

Superficial and deep adenopathies. When correctly irradiated from the outset, the enlarged lymph nodes or masses of nodes most often melt after a short latent period (fractional doses at frequent intervals); there is sometimes left a small fibrous residue, against which too stubborn therapeutic efforts should not be directed. Mediastinal adenopathy, even when quite large, may disappear completely and permanently (necropsy observations after many years in two of Gilbert's cases*). The lymph nodes in the abdominal cavity are

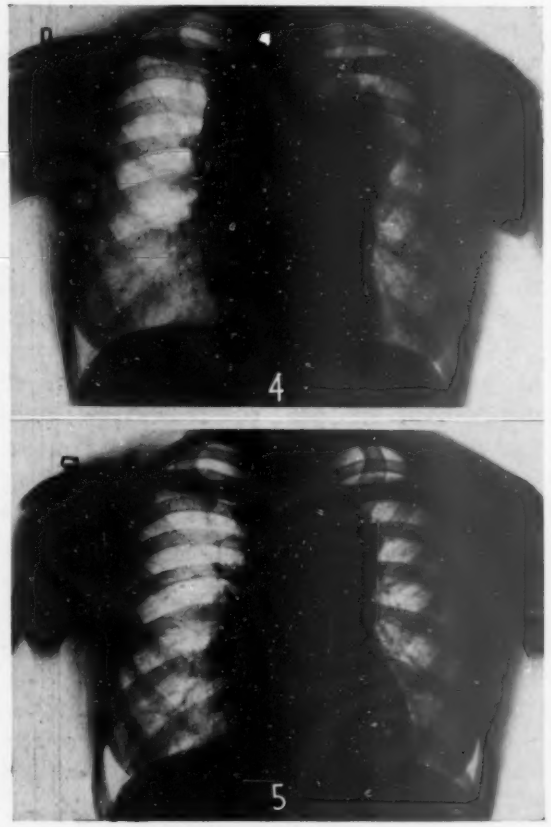
* Verified at the Pathologic Institute of the University (Prof. Askanazy).



Figs. 2 and 3. Case 1. Radiosensitive granulomatous tumor irradiated in 1922; free from local recurrence to date (1937).

more deceptive; difficult to discover, they are often irradiated too late, at an advanced stage of the disease; the patient's resistance has diminished, irradiation is not well tolerated, and cachexia has increased. Nevertheless, special cases may be encountered (Cases 1, 3, 16, etc.); in the first case, which was very radiosensitive, a serious recurrence with extension to the abdomen occurred in 1930; I regarded the patient as lost; a series of irradiations put him back on his feet, and he has remained well. The same thing occurred in Case 3, in which icterus, invasion of the retrocardiac space and pericardial friction rub developed; here recovery goes back only six months (twenty-four years' survival). Figures 4 and 5 give an example of a mediastinal tumor which was not very radiosensitive.

Infiltration of tissues other than lymph nodes (bones, spleen, lungs, serous membranes, cerebrospinal canal, etc.). Roentgen therapy is capable of inducing prolonged remissions, especially in cases of *bone infiltration*. The most common are vertebral or costovertebral foci, in which infiltrative extension occurs by contiguity with masses of paravertebral lymph nodes. When treated in time, they cease to be painful; in a goodly proportion of cases roentgen therapy proves that the destroyed bone can undergo repair (Cases 8 and 51; see Figs. 6, 7 and 8). Roentgen therapy can also overcome infectious metastases in the bone marrow where, by



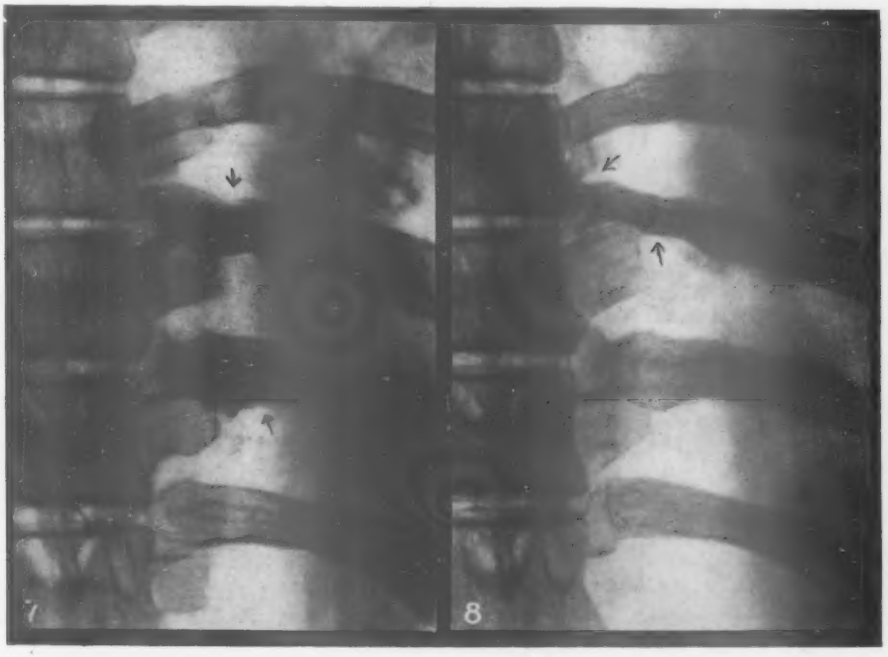
Figs. 4 and 5. Case 47. Moderately radiosensitive granulomatous tumor, after one year of evolution. Roentgenograms of March and April, 1935 (before and after roentgen therapy). Remission of eighteen months; recent and serious local recurrence (extension).

forming cavities, they may render the bone fragile. Sometimes roentgen therapy can cause only the subjective signs to disappear, but roentgenography shows the persistence of destructive changes observed previously; these foci, however, have become inactive; they may be watched for years without noting any increase; this would indicate that the destruction of the granulomatous tissues was complete (Case 8).

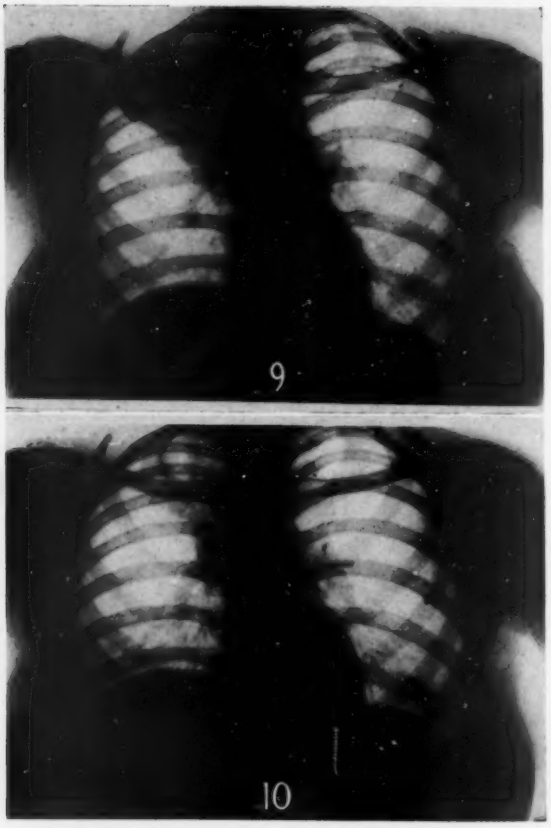
It is possible to destroy pulmonary infiltrations and to cause pleural effusion to disappear; but the results are difficult to obtain and are rather transitory (Figs. 9 and 10). In the event that the pathologic process has infiltrated the cerebrospinal canal, etc. (sphincteric disturbances, paresthesias, paraplegia), roentgen therapy, when applied in time, may cause these difficulties to recede; here also the action is often temporary; nevertheless, in Case 8, I obtained a survival of sixteen months from the time of medullary infiltration, with partial return to normal health (ability to walk, to work, etc.).

Fig. 6. Case 51. Destructive, costovertebral, granulomatous lesions; paravertebral shadow, probably lymph nodes. Status before roentgen therapy (June, 1933).

As for the spleen, it is not affected as often as has been claimed; usually spared in those regional forms in which the disease



Figs. 7 and 8. Same case: Fig. 7, in September, 1934; restoration of bone; Fig. 8, August, 1936; partial costovertebral recurrence again irradiated successfully.



Figs. 9 and 10. Case 10. Fig. 9, granulomatous infiltration of the lobe of one lung, occurring five years after the beginning of roentgen therapy (associated atelectasis?); Fig. 10, one month after roentgen therapy; regression followed by remission for eight months and by retractile fibrosis.

is confined to the cervical, axillary and upper thoracic lymph nodes, it is rarely involved by itself; most often, during phases of extension, the spleen becomes the site of infectious metastases.

The invasion of other viscera simulates what has been written concerning pleuropulmonary or spinal infiltration.

Effect on the general condition. Reaction. The indirect influence of segmental irradiation on the general condition of granulomatous patients, on recovery of strength, and on the improvement in nutrition, is remarkable. Figure 11 gives an extreme example of the influence of roentgen therapy on the weight curve (Case 13).

Fever and pruritus often coexist and respond to roentgen therapy in favorable forms. These two elements are a precious guide: if one or the other persists after wide irradiation of the clinically demonstrable manifestations (superficial and mediastinal adenopathy), it is because other foci remain to be neutralized. If abdominal exploration is negative, irradiation should be directed toward the zones most often silently invaded: the retroperitoneal, paraaortic lymph nodes, the spleen, etc.). Such increasingly extensive irradiation to larger and larger portions of the abdominal cavity should be made with care, keeping in mind the reactions of the general condition and of the blood. If clinical observation commands interruption of the treatment, resumption of it should be attempted after an interval of six weeks.

Sometimes, instead of subsiding after irradiation, the fever on the contrary may increase, especially if the doses are too high. This is the reef on which roentgen therapy founders (Beaujard). In average forms (dosage) this reaction should be avoided; otherwise, suspension of treatment may compromise a possible success.

Lowering of the temperature is a good sign; but it is wise to continue irradiation up to the usual minimal doses in order to avoid early recurrence by incomplete destruction of the granulomatous foci.

As for general reactions, these may be very slight if care is taken to test the susceptibility of the patient by beginning with rather small active doses (50 r at the level of the abnormal tissues), which may be doubled after a few days—which represents a surface dose of from 125 to 150 r for 180 kv. of homogeneous radiation and at a focal distance of 60 cm. (Schwarz, Gilbert). Clinical observations should guide the therapeutic radiologist.

Effects on the blood. When the blood picture is modified, segmental roentgen therapy exerts on it a remarkable influence. In the toxic anemic forms of granulomatosis, blood regeneration begins during the series of irradiations and continues steadily: Case 13 furnishes a typical example (rapid fall in leukocytosis, progressive in-

crease in the erythrocytes and hemoglobin, and reëstablishment of the leukocytic equilibrium). The chart of Case 7 (Fig. 12) at once indicates the influence of roentgen therapy and that of recurrences.

In obese patients segmental irradiation of the abdomen may provoke a transitory diminution of the erythrocytes; repeated blood counts prevent surprises of this kind.

to normal levels is a good prognostic sign; on the contrary, the existence of a high neutrophilic polymorphonuclear leukocytosis, and especially its resistance to roentgen therapy, have had a bad prognostic significance in my cases (Fig. 12).

As for the eosinophilic changes during treatment, these are very inconstant. An increase in the proportion of eosinophiles

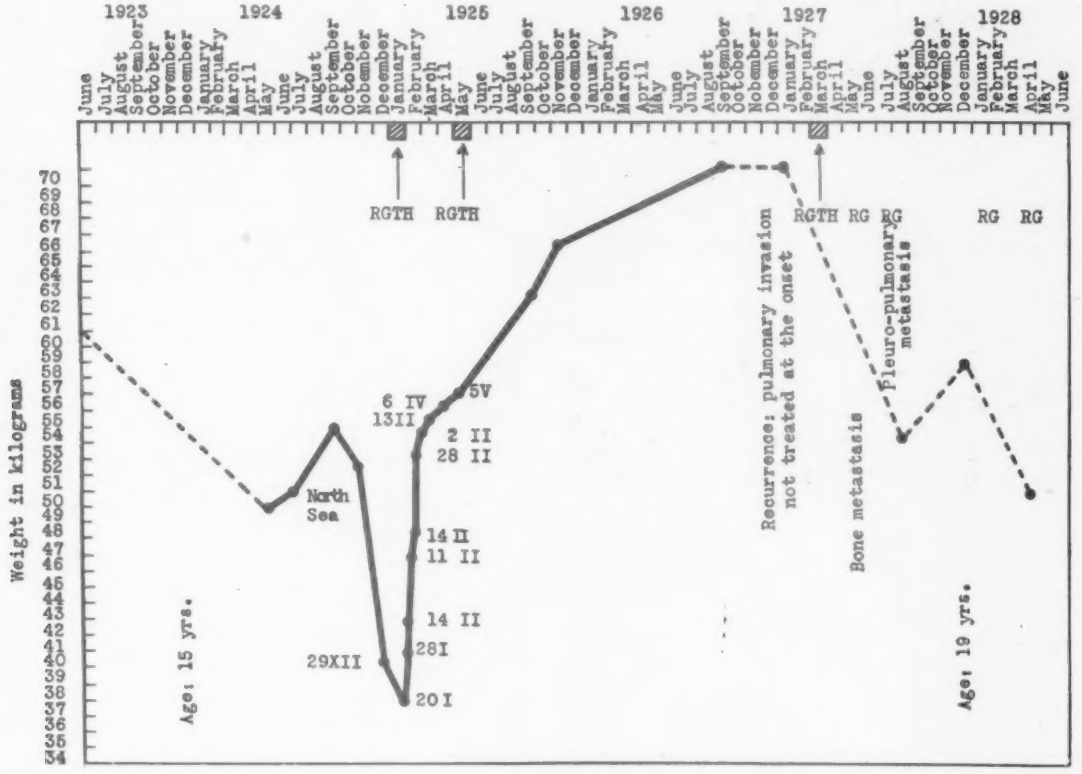


Fig. 11. Influence of malignant granulomatosis and of roentgen therapy on the weight curve in Case 7, from 1923 to 1928.

Leukopenia before irradiation is exceptional in Hodgkin's disease; it does not contraindicate roentgen therapy (Holthusen, Gilbert); with careful irradiation in such cases the number of leukocytes increases during treatment.

Usually, the leukocytosis yields to irradiation; a slow or incomplete fall may mean either the persistence of hidden but active foci of granulomatosis or sometimes, especially during the advanced stages, a certain degree of radioresistance.

The return of the leukocytic equilibrium

occurs frequently towards the end of irradiation, but in no way is it specific of granulomatosis. Askanazy wonders if this might not be a phenomenon related to the absorption of the altered tissues.

Altogether different are the reactions of the blood under the influence of total teleroentgen therapy. Here, despite doses (from 15 to 30 r) which, in segmental roentgen therapy, would be regarded as minimal, a reduction in the number of erythrocytes is sometimes observed after a latent period; this late and progressive anemia

can sometimes repair itself or may be repaired by repeated transfusion of 300 to 400 cc. of blood. Marchal and his coworkers (1934) counselled the immediate interruption of total irradiation when the erythrocytes fall to 3,000,000 or when the numeri-

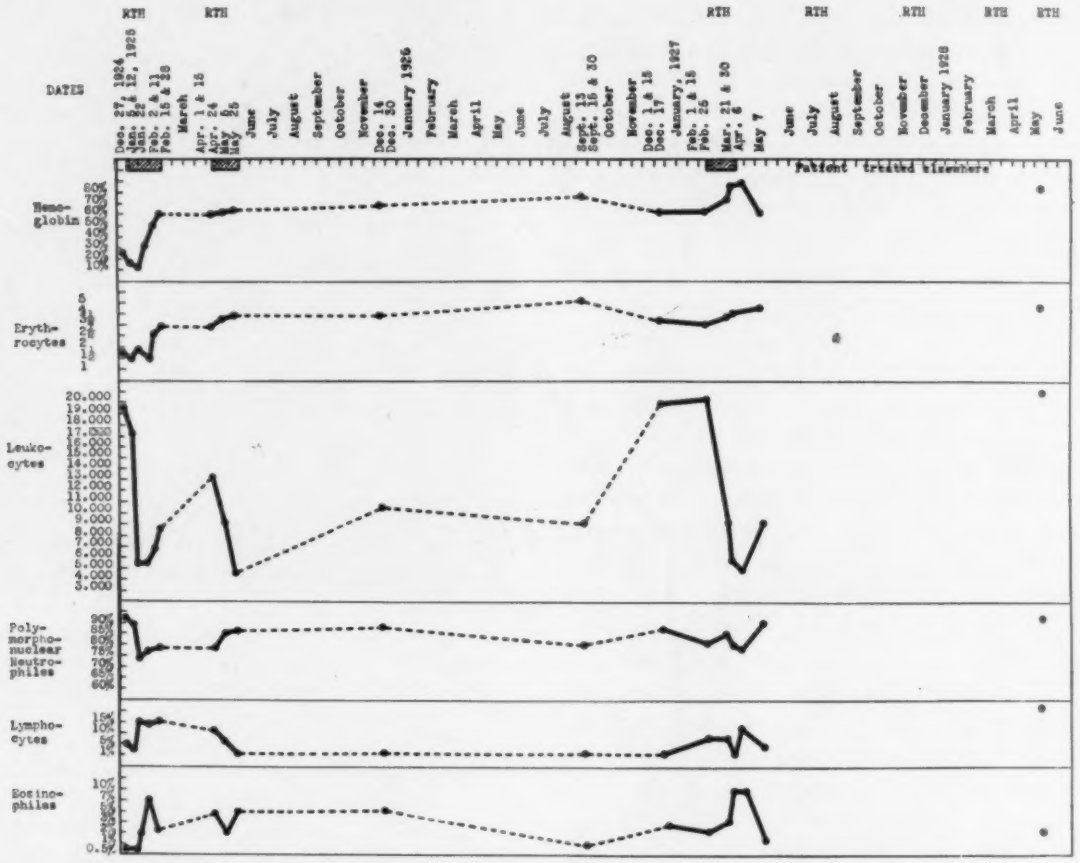


FIG. 12. Blood changes in malignant granulomatosis; influence of roentgen therapy (RTH) on the condition of the blood in a case of extreme toxic anemia (Case 7).

cal fall in cells is excessive (from 5,000,000 to 3,800,000 in one week, for example);* on the other hand, they observed that, when the leukopenia generally parallels the reduction in red cells, the leukopenia in Hodgkin's disease may be inconstant and capricious. Aubertin (1936) advised great care in the use of panteleroentgentherapy because of the risk of severe anemia. Moreover, we will see that the proofs of an efficacy comparable with that of segmental roentgen therapy are still lacking.

Effect on the ovaries. Gestation. When abdominal foci require irradiation of the ovarian region, an artificial menopause or temporary amenorrhea may follow, according to the age of the patient and the dose given; the patient should be forewarned. Given, on the one hand, the serious prognosis *quoad vitam* and the precarious therapeutic resources other than roentgen therapy and, on the other hand, the absence of proof of a noxious effect on the fetus, we are justified in irradiating a pregnant patient for granulomatosis. Sluys has done this successfully (seventh month).

As to the unfavorable influence of pregnancy on the evolution of malignant

* The destruction of blood cells may perhaps be due to the fact that total irradiation acts in only one direction on the entire hematopoietic system and, therefore, without compensatory reaction of the blood-forming organs which are spared by segmental roentgen therapy (Marchal and Mallet).

granuloma (Herz), I shall refer to it again and shall present some facts.

Accidents (effects on the skin, etc.). The ill-considered repetition of irradiation with slightly filtered rays, with fractional doses at long intervals required by early recurrence *in situ*, necessarily exposes the patient to accidents.

Penetrating roentgen therapy, with daily fractional doses destined to destroy the granulomatous foci at the very first course of treatment, has the capital advantage of being more active while diminishing the danger of local accidents. Thus, the repetition of roentgen therapy at more or less long intervals (months or years), as required by recurrence, is well tolerated provided the total doses are graded into series and provided moderate doses are given to radiosensitive forms of the disease. According to the complexion of the patient and the doses given, more or less pronounced pigmentation or temporary epilation may be observed. In Case 1 an enormous woody recurrence, which at first was resistant, occurred in the muscular masses adjoining the axilla and required two series of irradiations at short intervals with large total doses (cross fire); epilation of the axillary hollow, without any trace of telangiectasia, has persisted for six years.

Cross-fire irradiation of the thorax may cause pulmonary fibrosis (Evans and Leucutia, and one of Gilbert's cases). If the doses given at each series are graded, such exceptional accidents occur only at an advanced stage of the disease. Quite different are the early edematous reactions observed after massive irradiation of a mediastinal tumor (Czepa, Evans and Leucutia); these can be avoided by judicious fractionating of the dose.

The cardiac muscle demands certain precautions: Warthin and Pohle, in experiments on adult rats, have specified a threshold dose of about 500 r; in investigations on striated muscle in man, Englmann and Frank have shown that this is more radiosensitive than had previously been admitted; rather inconstant and partly reversible accidents have been noted for a depth dose of 2,400 r given in ten days. When irradiating the thorax, therefore, the choice of fields, the direction of the beams of rays, and the total depth dose should receive careful attention.

Finally, irradiation of the abdomen by the cross-fire method requires the usual precautions.

2. *Influence of Segmental Roentgen Therapy on the Clinical Forms.*

The classic form of granulomatosis at the outset is enlargement of lymph nodes in one or in many regions. It also may affect many regions, but disease in the peripheral nodes may predominate. Actually, segmental roentgen therapy can destroy all peripheral adenopathies and, in favorable forms, mediastinal or even abdominal adenopathy, to such a point that the results may be permanent and that, when recurrence develops, this involves other groups of nodes (paravertebral regions and certain abdominal groups), or certain viscera may be invaded. We can therefore see early forms undergo transformation into other clinical forms, sometimes after remissions of one to two years or longer. I shall not insist on these successive modifications of the clinical picture; they are multiple and individual because of the polymorphism of the disease.

3. *Influence of Segmental Roentgen Therapy on the Mode of Evolution.*

In the acute forms which evolve in a few weeks and which present unmistakable general signs this influence is almost nil. The rise in temperature, which is often intensified by roentgen therapy, commands the suspension of irradiation.

In rapid forms, in which the duration of the disease may extend from a *few months to two years*, roentgen therapy often has a favorable local effect, but it has little effect on the fatal evolution of the disease. Recurrence develops after brief delays and rapidly ends in general involvement.

Roentgen therapy may bring a respite and nothing more.

On the whole, the average chronic forms are the most common; their evolution extends from two to six years. It is in these forms that frank remissions of one or two years, or longer, with return to apparent health and to full working capacity, can be obtained. Often also roentgen therapy proves effective against recurrence, although the favorable effect is less and less lasting; at each phase of extension the disease involves more territory and becomes general; the patient dies in cachexia.

The greatest number of recurrences observed in any case was ten, and the smallest number, one (this last recurrence, which rapidly proved fatal, was in a woman aged seventy-eight—Case 22). The average number of recurrences is about three. Case 3 was referred to me *in extremis*, eighteen months after the appearance of the first symptoms. Roentgen therapy was being used for the first time. The patient could no longer eat, and her weight had fallen from 60 to 37 kg.; she had 1,700,000 erythrocytes, and, between the end of December and January 11, 1925, the hemoglobin fell from 28 per cent to 14 per cent, and then to 11 per cent. Segmental irradiation, which was cautiously started at the end of December, arrested the evolution of the disease and then enabled us to witness a real resurrection, with four years of survival, of which for two consecutive years the patient was apparently cured (Figs. 11 and 12).

In the average form the influence of roentgen therapy is also characterized by the fact that certain cases classed as average because of their clinical aspect at the beginning of roentgen therapy (febrile forms, etc., such as Case 8) may be prolonged beyond six years. Thus 5 patients from this group have been transferred to the group of cases characterized by a slow evolution (Cases 8, 10, 23, 24 and 31).

The forms which evolve slowly from the outset are relatively benign; roentgen therapy subdues them so well that we may almost speak of cure. In fact, 2 out of 3 of our oldest cases, which are still healthy after having survived twenty-four and sixteen years, respectively, have developed menacing recurrences: Case 3 had a second recurrence after an evolution of twenty-three years. A curious fact is that these 2 patients, who were well informed about the disease and whose periodic examinations had become less frequent, did not feel impelled to report their recurrences because they were certain that their physical difficulties were due to another disease; they consulted some one else, and we did not see them until several weeks later. Besides these forms others exist in which the recurrences develop at shorter intervals; witness Case 14. In certain patients as well as in the average form we have been able to subdue invaded abdominal nodes (long remissions), but such cases are a minority.

4. *Influence of Roentgen Therapy on Survival.*

Since Klewitz and Lullies, many authors have maintained that the duration of malignant granulomatosis was not influenced by roentgen therapy. This view which, on the basis of the results obtained fifteen years ago, seemed defensible is now known to be unwarranted. To be sure, the favorable results of roentgen therapy are relative and closely related to the evolutionary type, but the remissions with return to apparent health, obtained by many authors since the improvement in our methods of irradiation, are at once more frequent and of longer duration. Moreover, the improvement is *qualitative* as well as *quantitative*. This was justly expressed by McAlpin and Golden when they wrote: "We do not expect to cure, but hope to make life not only longer but happier."

Pregnancy. Before inspecting the figures I should like to develop an argument to support the progress realized during the past fifteen years concerning the duration of survival from the quantitative and qualitative points of view: this is the evolution of normal pregnancies in female

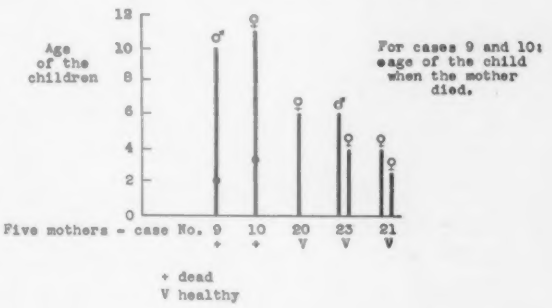
patients with granulomatosis in a state of remission after roentgen therapy. Of the 30 women in this first group (only 20 were aged between eighteen and forty-five), 5 have had one or two normal children. Besides these, Sluys and his coworkers reported in 1935 a case of granulomatosis discovered and treated during pregnancy (seventh month); the child was healthy, and the condition of the mother was satisfactory three years after confinement. In 2 cases the placenta, when examined histologically, did not show any sign of granulomatosis (Sluys, Gilbert). One of my patients nursed her baby *without my knowledge*. So also with the pregnancies; each time I was face to face with an accomplished fact. In Cases 9 and 10 recurrence developed subsequently, and the patients succumbed to generalized disease within from two to three and a half years. The 3 other mothers (five children) are alive: 2 had, during the late stage of pregnancy or immediately afterwards, a recurrence which was arrested by roentgen therapy; their births were not followed by recurrence. Of these 5 cases at least 3 clinically were of the average form; one has rejoined the two others in the group of cases with slow evolution of the disease. Thus, I believe I can assert that, here again, it is the evolutionary type, the degree of malignancy, which is most important; a secondary factor, no doubt, is the quality of remission obtained by roentgen therapy.

Patients suffering from granulomatosis should be advised against pregnancy as well as against marriage, but these events occur in spite of us. The interruption of pregnancy, as advocated by Herz, was not warranted in our cases. The question of the fate of the children is a more delicate problem because too little time has elapsed. Thus far, the seven children of my 5 granulomatous patients are all living and healthy in their phenotype; they are, respectively, in their twelfth, eleventh, seventh, seventh, fifth, fifth and third years (see Table 1). Five of the seven are females!

The question of possible injury to the genetic mechanism remains an open one, but this seems improbable: 2 of the mothers (Cases 10 and 23) had received, by abdominal irradiation, respective doses of approximately 700 to 900 r at the level of the ovaries; the amenorrhea lasted six months, and two and a half and one and a half years, respectively, elapsed between the last irradiation and the time of conception. In the 3 other patients, it had been possible to avoid pelvic irradiation.

TABLE I

CHILDREN BORN OF GRANULOMATOUS MOTHERS DURING POST-ROENTGENTHERAPEUTIC REMISSIONS (ALL WELL IN APRIL, 1937)



Today, therefore, it may justly be claimed that roentgen therapy exercises not only an undeniable influence on the quality and duration of the remissions, but also that it prolongs life.

5. Contraindications to Roentgen Therapy.

The acute forms and certain febrile forms with rapid evolution may force the suspension of roentgen therapy (exacerbations) or may force the radiologist to abandon it after trial.

The association of granulomatosis with a primary and active tuberculosis, especially if the latter should have a tendency to caseation, contraindicates irradiation of the lungs and mediastinum with the usual doses; this is also true in the event of renewed activity of tuberculosis after previous treatment. In our experience, such cases have seemed exceptional. In cases of mechanical difficulty by compression of the respiratory passages, however, palliative irradiation with a low out-

put in roentgens per minute, by means of small, well-directed beams, or by intra-esophageal radium therapy, may be resorted to.

Renal insufficiency and, still more, nitrogenic nephritis, contraindicate roentgen therapy; if necessary, treatment may be tried with great caution and with close attention to the blood urea.

Finally, deleterious effects of roentgen therapy may prove a contraindication, especially if the integrity of the skin has been compromised. Such cases should no longer be encountered and, fortunately, are becoming rare.

6. *Adjuvant Treatment.*

Treatment with rays of short wave length does not exclude adjuvant treatment, the object of which is to improve the general condition, on the one hand, and to diminish blood reactions, on the other hand.

Arsenical treatment is advised by many authors. Being opposed to prophylactic roentgen therapy, I often use arsenical treatment during periods of remission.

I have already mentioned the use of thorium X, which is debatable.

Against the anemia which often develops during the advanced stage of the disease, large doses of iron, calf's liver or liver extract (preferably by injection) are indicated.

We could not enumerate the many therapeutic tests which have been made or all the adjuvants which have been advocated.

During irradiation, the general condition of the patient should be kept under observation and hygienic measures prescribed (regular evacuation of the bowel, diuresis). A characteristic feature is that, in favorable cases, the general condition of granulomatous patients improves during the course of treatment; nevertheless, graduated heliotherapy and a tonic climate, such as an altitude of about 1,000 meters) may be advised after roentgen therapy as a convalescent measure, if circumstances permit; I have rarely made use of it.

Finally, in exceptional cases, surgery may be an adjuvant.

B. STATISTICAL RESULTS

Evaluation of the statistical results is a delicate matter. In interpreting the figures, it should be remembered that (1) roentgen therapy yields only remissions; (2) the evolutionary character of the disease plays a dominant rôle; (3) the method of treatment plays a large part in the results; (4) the expression "series of treatments" as well as the observation of isolated cases often lead us into erroneous generalizations in the direction of success as much as in that of failure.

As a reminder, I give the table which I published with Babaïantz and Kadrnka in 1934; this table gives a very imperfect idea of the clinical results observed. Later, I give the end-results. According to Voorhoeve, I have indicated not only the average duration of survival from the appearance of the first symptoms (DAPS) (this is necessarily arbitrary), but also the average duration of survival from the beginning of roentgen therapy (DART).

The results are very unequal (Table II); nevertheless, if the statistics are examined, they show a clear improvement during the last twenty years. The extreme figures *after the beginning of roentgen therapy* are one year and six months for 1917 and three years and nine months for 1937; the average varies between two and a half and three years. It should not be forgotten that the quality of the remissions should be added to the quantitative results.

As for the total duration of the disease, it runs from a minimum of one year and four months (1924) to a maximum of four years and six months (1937) if all the cases treated by each author are considered. It is therefore permissible to say that the duration of survival has doubled, and even tripled for certain authors. However, the table brings out appreciable differences for some renowned institutes; if the communications in question are analyzed, it is interesting to note that the respective pro-

TABLE II

Year of Publication	Authors	Number of Cases		Average Duration of Survival after Onset of Disease		
		Total	Utilizable	First Symptoms (DAPS)	Roentgen Therapy (DART)	
1917	Holding and Brown	18	10	—	1 yr. 10 mo.	
1917	Yates and Bunting	63	39	—	1 yr. 6 mo.	
1921	Colrat	13	—	—	2 yr. 9 mo.	
1921	Fraenkel	?	—	1 yr. 8 mo.	—	
1923	Chaoul and Lange	12	—	2 yr. 6 mo.	—	
1923	Naegeli	—	—	2 to 3 yr.	—	
1923	Desjardins	73	—	2 yr. 7 mo.	—	
1924	Schreiner and Mattick	46	—	2 yr. 7 mo.	—	
1924	Stone	164	—	1 yr. 4 mo.	—	
	of which	53	—	2 yr. 11 mo.		
1924	Klewitz and Lullies	24	16	—	1 yr. 8 mo.	
1924	Gillet	—	7	4 yr. 6 mo.	—	
1925	Voorhoeve (Group 1)	19	11	4 yr.	2 yr. 18 mo.	4
1926	Holthusen	32	—	2 yr.	—	6
1926	Desjardins	57	—	About 3 yr.	—	
1926	Burnam	173	9 living 110 dead	4 yr. 3 mo.	4 yr. 3 mo. 2 yr. 10 mo.	9
1927	Brugmann	20	4 rapid 8 chronic	¼ to ½ year. 2 yr. 8 mo.	— 2 yr. 8 mo.	
1928	Gilbert and Babaïantz (Group 1)	25	14	5 yr.	2 yr. 9 mo.	
1930	Billich	31	—	—	2 to 3 yr.	
1931	O'Brien	19	—	3 yr. 11 mo.	—	
1932	Holfelder and Hummel	56	52	3 yr. 5 mo.	2 yr. 5 mo.	
1932	Vesin	90	30	—	2 yr. 2 mo.	
1932	Goia	80	63	3 yr. 1 mo.	1 yr. 10 mo.	
1933	McAlpin and Golden	42	5 living 32 dead	5 yr. 10 mo. 2 yr. 8 mo.	— —	5
1934	Lecutia . . . (14 institutes)	805	—	—	From 2 to 3½ yr.	
1934	Gilbert, Babaïantz and Kadrnka (Group 1)	60	41	4 yr. 8 mo.	3 yr. 1 mo.	
1934	Smith	16 children	—	Approx. 3-5 yr.	—	
1935	Flax	54	14 living 40 dead	4 yr. 6.2 mo. 2 yr. 3.5 mo.	— —	14
1935	Melchart	15	—	3 yr.	—	
1935	Giordano and Salmeri	43	34	—	Approx. 2 yr.	
1936	Holfelder and Schultz	179	—	3 yr. 1.5 mo.	2 yr. 3 mo.	50
1936	O'Brien	45	11 living 34 dead	2 yr. 9 mo. 2 yr. 5 mo.	1 yr. 9.7 mo. 1 yr. 2.4 mo.	11
1936	Baensch	78	—	2 yr.	—	3
1937	Gilbert and Babaïantz (Group 1)	77	52	5 yr. 2.4 mo.	3 yr. 9.6 mo.	16
1937	Idem (Group 1 and 11)*	73	—	4 yr. 6 mo.	3 yr. 2.8 mo.	17

* See our detailed results in the tables and charts which follow.

portion of evolutionary types (rapid, average, slow) is subject to wide variations according to the regions involved: in Boston, O'Brien, who has adopted our classification, reports 60 per cent of rapid forms, 29 per cent of average forms, and 11 per cent of slow forms. In Frankfort the important study of Schultz enabled me to calculate, on the same basis, 31.9 per cent of rapid forms, 55.8 per cent of average chronic forms, and 12.3 per cent of slow forms. Therefore, my statistics of 1937, which are superior to those of 1934, give out of 52 cases (Group 1) 17.3 per cent of

Table III

GILBERT AND BABAÏANTZ (1920–1937)—GROUP I ACCORDING TO VOORHOEVE

Percentage Based on 52 cases	Survival after First Symptoms	Survival from Beginning of Roentgen Therapy	Survivors	Total No. of Cases
Acute and rapid forms 17.3%	1 yr. 1 mo.	7½ mo.	0	9
Average chronic forms 55.8%	3 yr. 7½ mo.	2 yr. 6½ mo.	8 28.6%	29
Slow forms or forms in which the disease has become chronic 26.9%	11 yr. 1 mo.	8 yr. 5 mo.	8 57%	14

rapid forms, 55.8 per cent of average chronic forms, and 26.9 per cent of slow forms or forms which became chronic after roentgen therapy (Table III).

Do obscure etiologic factors play a part? Does the accumulation of people in large cities engender unfavorable conditions, alimentation, etc.? The fact is that most of the forms which have become chronic (Cases 10, 24 and 28) have been in farmers living in the vicinity of Geneva, and that 3 of them—was this a coincidence?—came from the same village or its vicinity.

Another factor plays a part in the results; this is the extent of the disease at the beginning of roentgen therapy. The forms in which early generalization has occurred are the most difficult, especially when accompanied by fever and changes in the blood. Those in which involvement is confined to the upper part of the cervical region, on the contrary, yield the best remissions; when they develop slowly, it must not be forgotten that their character may suddenly change; it is wise, therefore, to treat them thoroughly until the general and local manifestations disappear completely. My best cases, which almost amount to cures, are of this kind.

I should also draw attention to the rôle of age in the quality of the results. An inspection of Tables IV, V, and VI is suggestive.

The most favorable forms belong, as a rule, to the third and fourth decades; after forty years, the disease usually assumes a more malignant character. Fifteen of our 17 survivors had become ill between twenty and forty years of age; and 32 of Schultz's 50 survivors belong to the same decades. The average age at which our cases (77) had become ill was 34.3 years; the average age of Schultz's 179 cases was 33.85 years.

The statistics by decades of Desjardins and Ford (1923) and of McAlpin and Golden (1931) give a similar age distribution. Other American statistics, on the contrary, give a higher percentage of older patients. For O'Brien, the average age of 28 men was 47.6 years, and that of 17 women was 40.6 years (with extreme figures approaching ours). Burnam, in 173

Table IV

DISTRIBUTION ACCORDING TO AGE AT ONSET OF THE DISEASE, AND ACCORDING TO SEX

	Average Age Males	Average Age Females	Average Age Total
Schultz (1936): 179 cases, of which 97 were males and 82 were females	36.04 yr.	31.65 yr.	35.85 yr.
Gilbert (1937): 77 cases, of which 38 were males and 39 were females	35.0 yr.	33.7 yr.	34.3 yr.

TABLE V

APPEARANCE OF THE FIRST SYMPTOMS, ACCORDING TO AGE AND SEX, IN OUR 77 CASES (39 MALES, 38 FEMALES)

Years	1–10		10–20		20–30		30–40		40–50		50–60		60–70		70–80	
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Dead	1		1	5	9	11	9	5	6	3	3	1	2	2		2
Both sexes	1		6		20		14		9		4		4		2	
Living				1	2	6	3	4		1						
Both sexes			1		8		7		1							
Total by decades	1		7		28		21		10		4		4		2	
Percentage of survivors by decades	0		14%		28.6%		33.3%		10%		0		0		0	

cases, found more than 22 per cent aged between twenty and fifty years; in 310 cases Craver noted an average age of thirty-four years for the patients who had survived more than five years (extreme ages: 6.5 and 67 years); and an average of 44.3 years (same extreme ages) for those who had survived six months or less. The chart published by Schreiner and Mattick (1924) is of the same order. Finally, in the cases reported by Flax (Zürich), 35 per cent fell between the fifth and sixth decades.

Thus, in contrast to malignant tumors, granulomatosis has a more rapidly fatal evolution after forty years of age, and statistics necessarily are influenced by it.

Besides the evolutionary character, the extent of the disease, and the age of the patients, the *method of irradiation* plays a certain part. This is proved by the distinct improvements reported by many authors during the past ten or fifteen years; Leucutia (1934), who gave us a synoptic study of the methods and results on the two con-

TABLE VI

COMPARATIVE FIGURES OF SCHULTZ (1936)

Years	1–10		10–20		20–30		30–40		40–50		50–60		60–70		70–80	
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Living	2	—	2	2	6	14	4	8	7	2	1	1	1	—	—	—
Both sexes	2		4		20		12		9		2		1		—	
Dead	2	—	6	17	21	22	17	11	16	9	8	3	5	—	2	—
Both sexes	2		13		43		28		25		11		5		2	
Total	4		17		63		40		34		13		6		2	
Percentage of survivors by decades	50%		23.5%		31.7%		30%		26.4%		15%		16.7%		0	

TABLE VII A

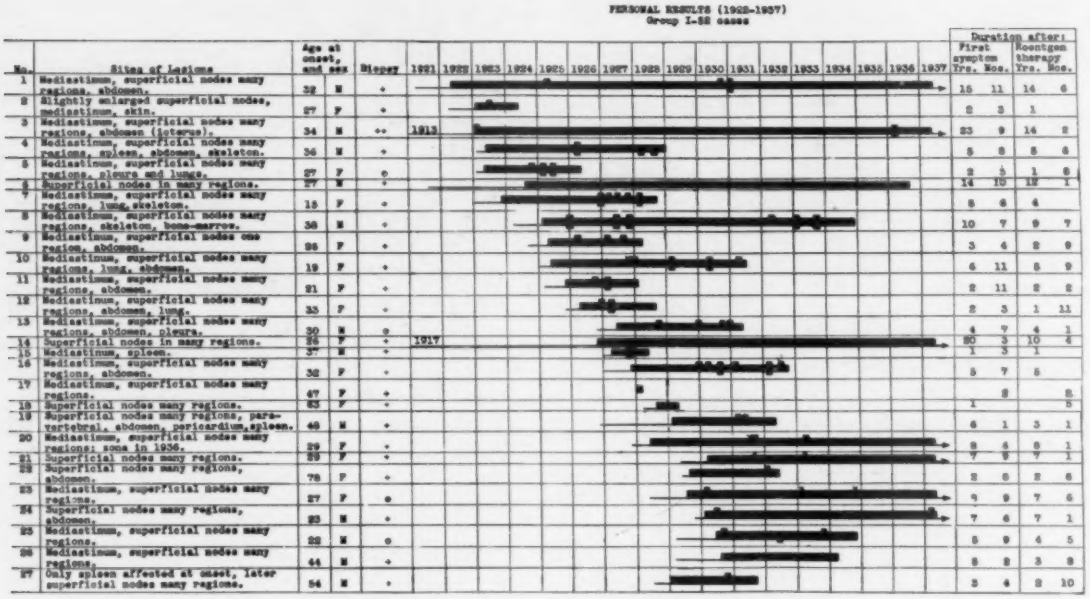
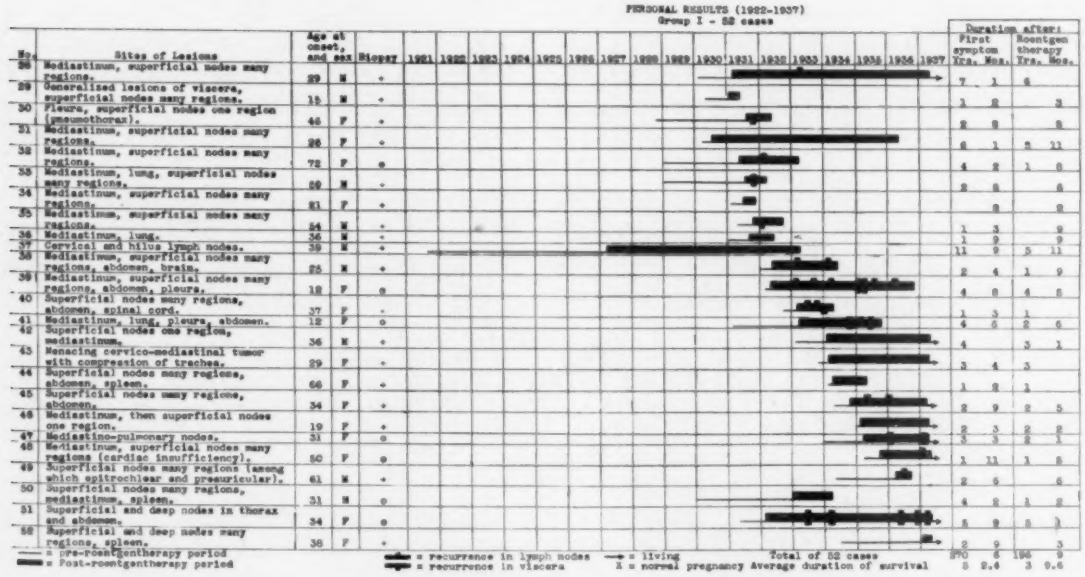
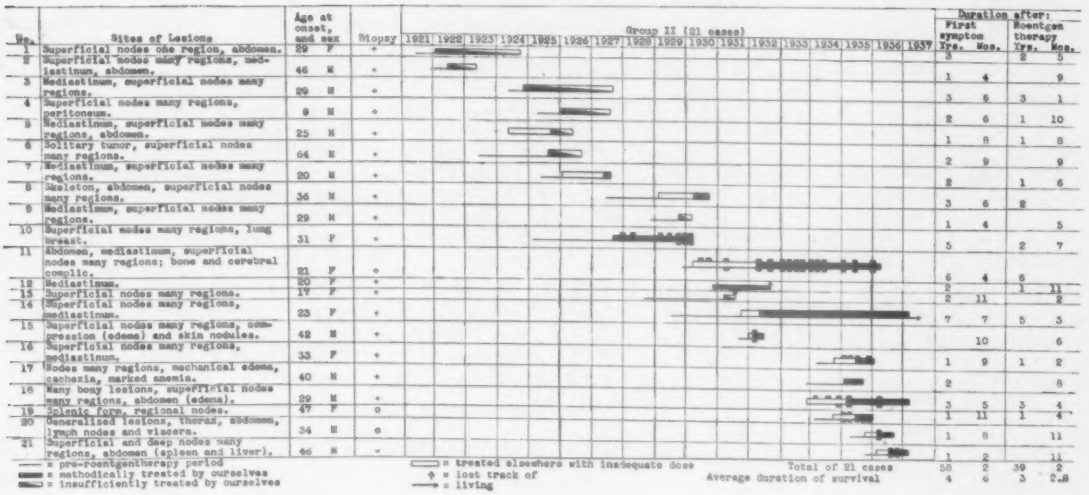

PERSONAL RESULTS (1922-1937)
Group I-52 cases
No.
Sites of Lesions
Age at onset, and sex
Biopsy
1921 1922 1923 1924 1925 1926 1927 1928 1929 1930 1931 1932 1933 1934 1935 1936 1937
Duration after:
First symptom Yrs. Mos.
Roentgen therapy Yrs. Mos.
1 Mediastinum, superficial nodes many regions, abdomen. 32 M + 15 11 14 6
2 Slightly enlarged superficial nodes, mediastinum, skin. 27 F + 2 3 1
3 Mediastinum, superficial nodes many regions, abdomen (icterus). 34 M ++ 1913 23 9 14 2
4 Mediastinum, superficial nodes many regions, spleen, abdomen, skeleton. 36 M + 5 8 5 6
5 Mediastinum, superficial nodes many regions, pleura and lungs. 27 F 0 2 5 1 8
6 Superficial nodes in many regions. 27 M + 14 10 12 1
7 Mediastinum, superficial nodes many regions, lung, skeleton. 18 F + 5 6 4
8 Mediastinum, superficial nodes many regions, skeleton, bone-marrow. 36 M + 10 7 9 7
9 Mediastinum, superficial nodes one region, abdomen. 24 F + 3 4 2 9
10 Mediastinum, superficial nodes many regions, lung, abdomen. 19 F + 6 11 5 9
11 Mediastinum, superficial nodes many regions, abdomen. 21 F + 2 11 2 2
12 Mediastinum, superficial nodes many regions, abdomen, lung. 35 F + 2 3 1 11
13 Mediastinum, superficial nodes many regions, abdomen, pleura. 30 M 0 4 7 4 1
14 Superficial nodes in many regions. 26 F + 1917 20 3 10 4
15 Mediastinum, spleen. 37 M + 1 3 1
16 Mediastinum, superficial nodes many regions, abdomen. 32 F + 5 7 5
17 Mediastinum, superficial nodes many regions. 47 F + 8 8
18 Superficial nodes many regions. 63 F + 1 8
19 Superficial nodes many regions, para-vertebral, abdomen, pericardium, spleen. 40 M + 6 1 3 1
20 Mediastinum, superficial nodes many regions; soma in 1936. 29 F + 8 4 8 1
21 Superficial nodes many regions. 59 F + 7 9 7 1
22 Superficial nodes many regions, abdomen. 78 F + 2 8 2 6
23 Mediastinum, superficial nodes many regions. 27 F 0 9 9 7 6
24 Superficial nodes many regions, abdomen. 23 M + 7 6 7 1
25 Mediastinum, superficial nodes many regions. 22 M 0 5 9 4 5
26 Mediastinum, superficial nodes many regions. 44 M + 8 8 3 8
27 Only spleen affected at onset, later superficial nodes many regions. 54 M + 3 4 2 10
= pre-roentgentherapy period
= Post-roentgentherapy period
= recurrence in lymph nodes
= recurrence in viscera
= living
= normal pregnancy
Total of 52 cases
Average duration of survival
170 6 196 9
3 2.4 3 9.6

TABLE VII B


PERSONAL RESULTS (1922-1937)
Group I - 52 cases
No.
Sites of Lesions
Age at onset, and sex
Biopsy
1921 1922 1923 1924 1925 1926 1927 1928 1929 1930 1931 1932 1933 1934 1935 1936 1937
Duration after:
First symptom Yrs. Mos.
Roentgen therapy Yrs. Mos.
28 Mediastinum, superficial nodes many regions. 29 M + 7 1 6
29 Generalised lesions of viscera, superficial nodes many regions. 15 M + 1 8 3
30 Pleura, superficial nodes one region (pneumothorax). 46 F + 2 9 2
31 Mediastinum, superficial nodes many regions. 26 F + 6 1 2 11
32 Mediastinum, superficial nodes many regions. 72 F 0 4 2 1 6
33 Mediastinum, lung, superficial nodes many regions. 29 M + 2 8 6
34 Mediastinum, superficial nodes many regions. 21 F + 2 2
35 Mediastinum, superficial nodes many regions. 54 M + 1 3 9
36 Mediastinum, lung. 36 M + 1 3 9
37 Cervical and hilus lymph nodes. 39 M + 11 9 5 11
38 Mediastinum, superficial nodes many regions, abdomen, brain. 25 M + 2 4 1 9
39 Mediastinum, superficial nodes many regions, abdomen, pleura. 18 F 0 4 8 4 6
40 Superficial nodes many regions, abdomen, spinal cord. 27 F + 1 3 1
41 Mediastinum, lung, pleura, abdomen. 12 F 0 4 6 2 6
42 Superficial nodes one region, mediastinum. 36 M + 4 3 1
43 Menacing cervico-mediastinal tumor with compression of trachea. 29 F + 3 4 3
44 Superficial nodes many regions, abdomen, spleen. 66 F + 1 8 1
45 Superficial nodes many regions, abdomen. 34 F + 2 9 2 5
46 Mediastinum, then superficial nodes one region. 19 F + 2 3 2 2
47 Mediastino-pulmonary nodes. 31 F 0 3 3 2 1
48 Mediastinum, superficial nodes many regions (cardiac insufficiency). 50 F 0 1 11 1 8
49 Superficial nodes many regions (among which epitrochlear and preauricular). 61 M + 2 6 6
50 Superficial nodes many regions, mediastinum, spleen. 31 M 0 4 8 1 2
51 Superficial and deep nodes in thorax and abdomen. 34 F 0 5 9 3 3
52 Superficial and deep nodes many regions, spleen. 36 F + 2 9 3
= pre-roentgentherapy period
= Post-roentgentherapy period
= recurrence in lymph nodes
= recurrence in viscera
= living
= normal pregnancy
Total of 52 cases
Average duration of survival
170 6 196 9
3 2.4 3 9.6

tinents, has brought them into the light. The technical progress seems to consist of a better distribution of depth dose and of doses of radiation sufficiently *large and active* to destroy all the granulomatous foci. Holfelder and Schultz, whose statistics are the most important in Europe, give us valuable indications on the importance of dosage; after having long tried to obtain results with "*the smallest possible, active doses*" (fractional), they found themselves obliged to increase these doses more and more as the disease continued to evolve, in order to obtain remissions; during the last period, they decided to use more active doses from the start, doses appreciably larger than those previously employed; in spite of the short time which has elapsed,

TABLE VIII


Group II (21 cases)
1921 1922 1923 1924 1925 1926 1927 1928 1929 1930 1931 1932 1933 1934 1935 1936 1937
= pre-roentgentherapy period
= methodically treated by ourselves
= insufficiently treated by ourselves
= treated elsewhere with inadequate dose
= lost track of
= living

No.	Sites of Lesions	Age at onset, and sex	Biopsy	Duration after: First symptom Yrs.	Mos.	Roentgen therapy Yrs.	Mos.
1	Superficial nodes one region, abdomen.	29 F	+	8		2	5
2	Superficial nodes many regions, mediastinum, abdomen.	46 M	+				
3	Mediastinum, superficial nodes many regions.	29 M	+	1	4		9
4	Superficial nodes many regions, peritoneum.	9 M	+	3	6	3	1
5	Mediastinum, superficial nodes many regions, abdomen.	25 M	+	2	6	1	10
6	Solitary tumor, superficial nodes many regions.	64 M	+	1	8	1	8
7	Mediastinum, superficial nodes many regions.	20 M	+	2	9		9
8	Skeleton, abdomen, superficial nodes many regions.	36 M	+	2		1	6
9	Mediastinum, superficial nodes many regions.	29 M	+	3	6	2	
10	Superficial nodes many regions, lung breast.	31 F	+	1	4		5
11	Abdomen, mediastinum, superficial nodes many regions; bone and cerebral complic.	21 F	+	5		2	7
12	Mediastinum.	20 F	+	6	4	6	
13	Superficial nodes many regions.	17 F	+	2		1	11
14	Superficial nodes many regions, mediastinum.	23 F	+	2	11		2
15	Superficial nodes many regions, compression (edema) and skin nodules.	42 M	+	7	7	5	3
16	Superficial nodes many regions, mediastinum.	33 F	+		10		6
17	Nodes many regions, mechanical edema, cachexia, marked anemia.	40 M	+	1	9	1	2
18	Many bony lesions, superficial nodes many regions, abdomen (edema).	29 M	+	2			8
19	Splenic form, regional nodes.	47 F	0	3	5	3	4
20	Generalized lesions, thorax, abdomen, lymph nodes and viscera.	34 M	0	1	11	1	4
21	Superficial and deep nodes many regions, abdomen (spleen and liver).	44 M	-	1	8		11
				1	2		11
				58	2	39	2
				4	0	3	2.8

Total of 21 cases
Average duration of survival

TABLE IX

RECAPITULATION

77 cases (observed from April, 1920 to March, 1937, or:

4 cases of 1920–1921 treated with roentgen therapy of little penetration and small doses repeated at long intervals.

From the appearance of the first symptoms (=DAPS): about 2 yr. 2 mo.
From the beginning of roentgen therapy (=DART): about 1 yr. 6 mo.

73 cases (1922–1937) treated with deep roentgen therapy with daily fractional doses of which:

I. *52 cases treated systematically*

DAPS 5 yr. 2.4 mo.
DART 3 yr. 9.6 mo.

16 living cases (30.8%)

DAPS 8 yr. 2 mo.
DART 6 yr. 4 mo.

36 dead cases

(69.2%)
DAPS 3 yr. 11 mo.
DART 2 yr. 7.3 mo.

Evolutionary varieties in relation to roentgen therapy:

acute: 1 case
rapid: 8 cases } 17.3%
average: 29 cases 55.8%
slow: 14 cases 26.9%

Total: 52 cases (100%)

II. *21 cases that could not be treated systematically, early or later:*

DAPS 2 yr. 9.2 mo.
DART 1 yr. 10.3 mo.

(a) Treatment begun elsewhere (fragmentary application in time or space), or treatment interrupted for reasons independent of the disease: 19 cases

(b) Cases lost track of 2 cases

of which 1 case living, with slow evolution (No. 14)

Groups I and II together (73 cases)

DAPS 4 yr. 6 mo.
DART 3 yr. 2.8 mo.

TABLE X

Forms with Slow Evolution	Number of Cases	Survival after Appearance of the First Symptoms
Goia cases not irradiated	12	7 yr. 1 mo.
Gilbert (March, 1937*) cases irradiated	14	11 yr. 1 mo.

* At the end of 1933, I reported with Babaïantz and Kadrnka: 8 cases with a survival of 11 years and 7 months. Of the 6 new cases from evolutionary Group C 5, according to our observations and prognostications, owe this transfer to roentgen therapy.

they consider their initial results more satisfactory. In fact, it may be mentioned that of 179 cases they announced 50 survivors, of which 22 were in a state of apparent cure, with full working capacity. From Schinz's Institute, Flax reports an improvement in results during the last few years and attributes it to technical advances as well as to the principles followed in the method of irradiation.

The diagnosis is based on a histologic examination (a biopsy as a rule) in 82 per cent of the cases. In the other cases the clinical diagnosis and the course of the disease were characteristic. A few doubtful cases have been eliminated.

The cases are divided into two groups according to Voorhoeve: Group I, cases correctly treated, and Group II, cases that had not received systematic treatment (for various reasons *independent of the disease*). To eliminate any semblance of artifice, I also give the results in both groups taken together (73 cases); only the 4 cases treated before the advent of deep roentgen therapy are not included.

TABLE XI

SCHULTZ (1936): ALL CASES, OR 179 (1920–1935)

PATIENTS WHO HAVE LIVED MORE THAN A YEAR SINCE THE BEGINNING OF THE DISEASE

	Years											
	13	10	9	8	7	6	5	4	3	2	1	0
Cases living	1	1	2	3	3	2	3	10	2	6	11	6
Cases dead	—	—	—	1	2	—	3	5	12	15	33	58

The average duration of survival in my cases has been favorably influenced by a fortunate proportion of moderate evolutionary forms, but I believe the method of irradiation which I have employed successfully for fifteen years has contributed to this result.

My own results will be found in the charts and tables.

These charts and tables contain *all the cases* of malignant granulomatosis which have been referred to me for treatment, without any selection.* They are an extension of the charts which I and my collaborators have published periodically since 1928.†

The principal sites of disease are mentioned; also the appearance of recurrence, and the surprise of 7 births! The evolution of the disease before and after roentgen therapy is recorded in definite figures (DAPS and DART). A general table (Table IX) permits one to compare the partial and total results. Finally, I give the comparative results for the slow forms, irradiated and not irradiated (Table X), and the late or long-range results (Tables XI to XIII).

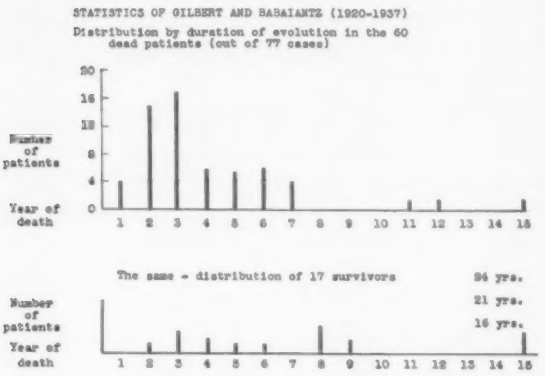
"Series" as a Factor. In 1931 we had 7 consecutive cases of the rapid form of the disease; this had never occurred during the eight previous years and has not occurred

* Forty-five cases were treated at the University Institute of the Geneva Cantonal Hospital; 32 cases are private patients (Institute of the Geneva General Clinic).

† In the course of this review I found 3 old cases, one of which had been recorded as "not heard from," and I rectified two errors. With these exceptions the numbers of 1934 remain unchanged. The ages given are those at the onset of the disease.

since. Also, in fifteen months and during the course of recurrences, we had 3 cases (Cases 8, 38 and 40) in which the central nervous system was involved, and soon thereafter a case with the late complication of mental confusion (Case 11)—observations which had never been made during the thirteen previous years (in 60) and which have not been seen since that time.

TABLE XII


STATISTICS OF GILBERT AND BABAIANTZ (1920-1937)
Distribution by duration of evolution in the 60 dead patients (out of 77 cases)
Number of patients
Year of death
The same - distribution of 17 survivors
26 yrs.
21 yrs.
16 yrs.

The same for the sexes: from Cases 39 to 48 we find 1 male and 9 females; the variations between the two sexes periodically tend to come into balance; at the present time we count 39 males and 38 females.

These observations show how cautious one must be in evaluating the results.

CONCLUSIONS

1. Malignant granulomatosis (synonyms: lymphogranulomatosis, Hodgkin's disease), in spite of low frequency, presents much interest from the double point of view of diagnosis and therapeusis.

Roentgenologic exploration offers a valuable means of orienting clinical diagnosis, of determining the site and extent of certain deep lesions, of verifying and following their regression after treatment or their extension after recurrence.

In the absence of any treatment based on etiology, systematic roentgen therapy constitutes the therapeutic method of choice because, by reason of the essentially lymphoid character of its lesions, malignant granulomatosis usually has an exceptional degree of radiosensitiveness.

2. The diagnosis should be made as early as possible and should rest on a biopsy whenever this is possible; the certainty thus obtained, especially in clinically doubtful cases, is essential to correct and early treatment.

3. In this very special systemic disease, the therapeutic radiologist must act as a general physician; he should know well the manifestations of the disease and the regions involved by it, its modes of extension,

TABLE XIII

LONG TERM RESULTS

(Patients who have survived more than 3 and 5 years, respectively)

Authors and Years of Publication	Period of Observation	Number of Cases	Number and Percentage of Surviving Patients	
			More than 3 yr.	More than 5 yr.
Desjardins and Ford (1923)	1915–1920	73	10 = 13.7%	7 = 9.8%
Holfelder and Hummel (1932)	1920–1939 resp. 1927	52 45	19 = 36.6%	8 = 17.7%
Gilbert and Babaïantz (IV–1937)	1920–1934 resp. 1932	46 38	21 = 45.7%	13 = 34.2%

Desjardins and Ford specified that the cases observed between 1915 and 1920 had received a variety of treatments, but *no systematic treatment*.

After 1920, on the contrary, the results concerned cases submitted to systematic treatment (roentgen therapy).

It may be stated that the proportion of long-term results had approximately tripled and that it reflects the progress in irradiation technique accomplished since 1920.

its types and evolutionary caprices, and naturally the mode of action of roentgen therapy as well as the reactions of the patient during treatment. The therapeutic radiologist should not content himself with treating isolated superficial regions (obvious adenopathies, for instance); his task is to "track the disease in all its haunts." It is on this basis that he should establish a plan of treatment the execution of which will remain subordinate to the evolution of each case.

4. The biologic effect of segmental roentgen therapy on the granulomatous tissues is essentially direct, destructive (cytolytic), whatever the site of the lesions may be and whether they are within or without the lymph nodes; this direct effect is followed by a fibrous connective tissue process which appears as an activation of the spontaneous process often observed when the disease is allowed to go untreated. When they occur, local recurrences start from residual islands of granulomatous tissue often due, during the first phase of radiosensitive forms of the disease, to inadequate doses.

5. The aim of treatment is to obtain as frank and as long remissions as possible, thus restoring to the patient the illusion of recovered health and complete capacity to work. This implies the methodical destruction of all the granulomatous foci, deep and superficial, without jeopardizing the general condition of the patient or the condition of the blood.

6. Except in special cases, roentgen therapy is more important than radium therapy because of the extent of territory to be irradiated and because of the doses to be delivered to the deepest foci.

Segmental roentgen therapy has proved its worth and is the method of choice; panteleroentgen therapy in this disease seems contraindicated.

Technique. Penetrating roentgen therapy: 170 to 200 kv.; filtration through 0.5 mm. to 1 mm. of copper and 1 mm. of aluminum, with a half-layer value of at least 0.9 mm. of copper; focal distances varying between 35 and 60 cm.; large fields, up to 400 sq. cm.; the whole aiming toward a better transmission output.

Simple, daily, fractional irradiation directed to each invaded region in succession or, according to the cases, directed first to regions requiring the earliest treatment. Thanks to the rotation plan, each field is irradiated only at intervals of about two days until a sufficient total dose has been given (clinical and blood examinations). Fractioning of the dose to each field over a period of ten to fifteen days; duration of the treatment, about five weeks (see details in the text).

7. *Repetition of roentgen therapy:* only on the appearance of recurrence. So-called "maintenance" or prophylactic treatment is superfluous and even detrimental. On the contrary, careful, periodic examination of treated patients, in order to intervene at the proper time.

8. The results of roentgen therapy are examined from the clinical and statistical aspects. Regression of the principal symptoms is known. The treatment modifies the clinical aspect of the disease and retards its evolution. The influence of roentgen therapy is the more pronounced as the disease is less malignant; its extent and the age of the patient also are factors.

Allowing for these factors, the method of irradiation clearly contributes to successful treatment; the advances of the past fifteen years furnish ample evidence.

The average duration of survival is incontestably prolonged; according to different authors, the period of survival has doubled and even tripled; the same proportion is found *when the long term results* are analyzed. To these quantitative elements should be added the quality of the remissions: in the average chronic and in the slow forms these assume the character of a clinical cure with full capacity to work; besides, pregnancies, even though they may have been discouraged, proceed without incident during periods of remission after treatment; the children are alive and healthy.

Thus, like the clinician, the therapeutic

radiologist must not allow himself to be discouraged by failures, several of which may occur in successive cases; on the contrary, he should use methodically the only weapon capable of crowning his efforts with success by improving the fate of his unfortunate patients.

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RESULTS OF ILIAC LYMPHADENECTOMY WITH IRRADIATION IN BORDERLINE CANCER OF THE CERVIX*

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EVER since radical operative methods for the treatment of cancer of the cervix were begun forty years ago, the question of the frequency and treatment of lymph gland metastasis in this type of malignancy has been a subject of debate. From extensive pathologic studies made then and since that time by Brunet, Baisch, Kundrat, Schauta, Mackenrodt, Lahm, Leveuf, Bonney and others, it has been shown that lymph gland metastasis occurs with increasing frequency in proportion to the extent of the local involvement. Using the League of Nations classification for cancer of the cervix, the figures are approximately as follows: Group I, 15–25 per cent lymph gland involvement; Group II, 30–40 per cent involvement; Group III, 50 per cent involvement; Group IV, 60 per cent involvement; at autopsy 66 per cent involvement.

Radium therapy has proved of great value in the destruction of the primary seat of the disease and its extension to the surrounding lymph spaces. When, however, the cancer cells are transported to the tissues of the lymph glands, they become, for some unknown reason, more resistant to radiation. Even the direct implantation of radon seeds or radium needles into the glands has usually failed to produce complete destruction. Hence cancer therapists have felt compelled to resort to surgical ablation of the tributary lymph glands to effect a cure in these cases. The technical difficulties involved in such a lymphadenectomy may be great and the primary mortality, if combined with extensive local excisions, is very high.

This has deterred many gynecologists from taking up the surgical attack except in the early Group I cases. Results in these early cases whether by irradiation or by surgery are reasonably satisfactory, but unfortunately they number only a small percentage. My special interest in recent years has been in improving results in the borderline or Group II cases, which are at least two or three times as numerous. In this group many observers report an adequate number of local regressions with irradiation, but a disappointingly large percentage of recurrences in the lateral pelvic region due to lymph gland metastases.

My proposal, therefore, was to treat the local site of the disease in the cervix by irradiation and to accompany this by surgical removal of the tributary obturator-hypogastic lymph gland chain from above. The first operation of this kind was done in October, 1930, and up to May, 1937, I have employed this method of treatment in 66 cases. The technique of the operation has undergone only minor modifications during this time. In the first two years I attempted this procedure in a few Group III cases but the high mortality and failures to give relief made me abandon its use for these more advanced cases. In 3 patients I found on laparotomy that the cancerous lymph glands were all so densely adherent to the large vessels that their removal was impossible. I did not include these 3 cases in my series.

There were 2 operative deaths in these 66 iliac lymphadenectomies, a primary mortality of 3 per cent. In both instances the postoperative death may, with reasonable probability, be attributed to the coincidental radium treatment. One patient, in whom radon seeds were implanted in the tissues next to the uterine vessels, died suddenly on the seventh day from pul-

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

monary embolus. The other postoperative fatality was due to peritonitis on the sixth day. This patient had a rudimentary left uterine horn which was removed with the adnexa of the same side. After closing the abdomen, radium was applied from below but the 50 milligram tube inserted into the uterine cavity (as shown by the autopsy findings) must have partly penetrated into the broad ligament. From the necrotic infected slough at this point a fatal peritonitis developed. Since this time (Nov. 2, 1935) no radiation treatment has been given at the time of the operation, and in the last 32 cases treated since then there has been no operative death. I am convinced, therefore, that, if done as a separate procedure, and, if limited to those Group II cases that present no surgical contraindications, the operation of iliac lymphadenectomy is attended by no appreciable risk. The arguments made against the radical Wertheim hysterectomy with gland removal because of its high primary mortality do not apply to the gland removal operation alone. The deaths in these extensive operations must be attributed to the shock of the long operation, the greater chance of infection, and the frequency of injury to neighboring organs, factors that are not present in iliac lymphadenectomy.

Due care in the selection of cases is important. Women over sixty years of age, those having high blood pressure, renal or cardiac lesions, those with obese abdominal walls, diabetics, and other bad surgical risks have not been subjected to operation. A few patients refused surgical intervention. At the Barnard Free Skin and Cancer Hospital, where all but four of my cases were operated on, the service was up to one year ago divided into six-month periods between Dr. Gellhorn and myself. During Dr. Gellhorn's service until his death in January, 1936, all Group II cases were treated by irradiation alone. This permitted a fair comparison with the results of my combined method of treatment, as will be shown subsequently in the survival curves of the two series of cases.

Since younger individuals were, as a rule, in better condition for operation, it is not surprising that the age of patients in my series was lower than the average for all cervical cancer cases (forty-three years compared with forty-nine years). Forty-three per cent of my patients were under forty years of age compared to the usual proportion of only 26.5 per cent for all cervical cancer cases. It is usually stated that in younger individuals there is greater tendency to lymph gland metastasis but this was not true in our small group, since the average age of those showing glandular metastasis was identical with those showing none. In fact the survival rate in the younger individuals was a trifle better than that of older individuals.

A total of 347 glands were removed in the 66 cases, an average of over five glands for each case. With improvement in our technique the number of glands removed increased in number so that at present from seven to ten glands are excised with their surrounding fatty areolar tissue. No attempt has been made to adopt the technique suggested by Leveuf and Godard and remove them as a unit. Such a procedure is unnecessarily time consuming and practically impossible, because of the tenuous connection between the lymphatic chain. The object has been to remove the glands and fatty tissue at the bifurcation of the iliacs, the glands along the obturator nerve up to the obturator foramen, and the lymph-bearing areolar tissue covering the external iliac vessels up to Poupart's ligament. Occasionally if a ureteral lymph node is palpably enlarged, time is taken to dissect it free from ureter and uterine vessels, but this is not done routinely, since it adds considerably to the risk of hemorrhage and the duration of the operation. In about half a dozen cases the uterine vessels were ligated according to the suggestion of Duncan, but I have recently abandoned this because it lowers the resistance of the normal tissues in the cervix to further irradiation and hence increases and prolongs the radium necrosis in the cervix.

Many sections were made from each one of the 347 glands removed and their study brought out many interesting points. The recognition of a small cancer metastasis in the lymph glands is very difficult owing to the frequency with which we normally find small nests of epithelioid cells and the necessity of serial sections to avoid missing some involved area. I am convinced that preliminary irradiation, especially deep roentgen therapy, increases the difficulty of recognizing metastases. While the numbers are too small to be of significance, cancer metastases were found in 4 out of 10 patients that had had no preoperative irradiation, whereas in the remaining 56 cases who had preliminary roentgen or radium irradiation the number with cancer metastases was only 18, that is 40 per cent as compared with 32 per cent. Thus, we had a total of 22 lymph gland metastases in the 66 cases of iliac lymphadenectomy ($33\frac{1}{3}$ per cent). I have rigidly excluded all doubtful cases, among which are 2 which in my first publication in 1934 I included as cancer metastases.

The attack on the cancer was three-fold: (1) deep roentgen therapy; (2) radium treatment; (3) surgery. There was some variation in the order in which these three measures were applied, depending on external conditions, but in general the preferred technique as at present adopted consists of: (1) 4,000–5,000 r deep roentgen rays administered under the direction of Dr. E. C. Ernst over a period of three weeks; (2) two or three weeks after the conclusion of the roentgen treatments a typical double-sided iliac lymphadenectomy; (3) two or three weeks after the laparotomy a radium application of 100–150 mg. of radium, filtered with 2 mm. of gold, to the uterine cavity and cervix for a total dosage of 4,500 mg-hr.

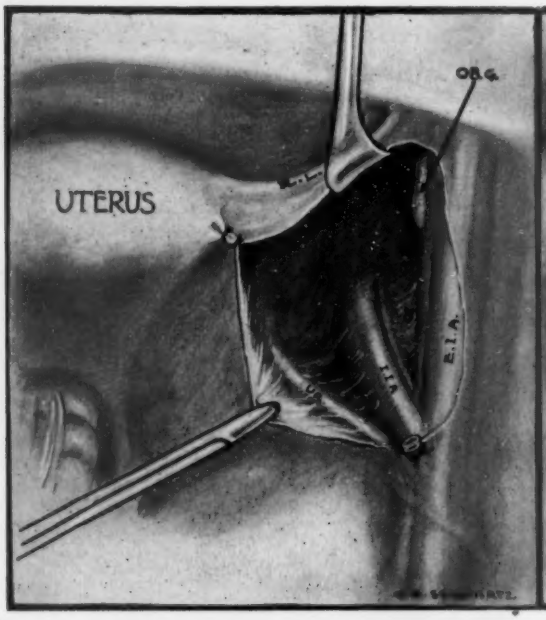

FIG. 1. Iliac lymphadenectomy. Exposure for removing hypogastric and obturator glands. Hypogastric gland has been removed. Obturator gland (*OB.G.*) visible in the angle between the external iliac artery (*E.I.A.*) and internal iliac artery (*I.I.A.*) with the ureter (*UR.*) attached to the posterior layer of the broad ligament.

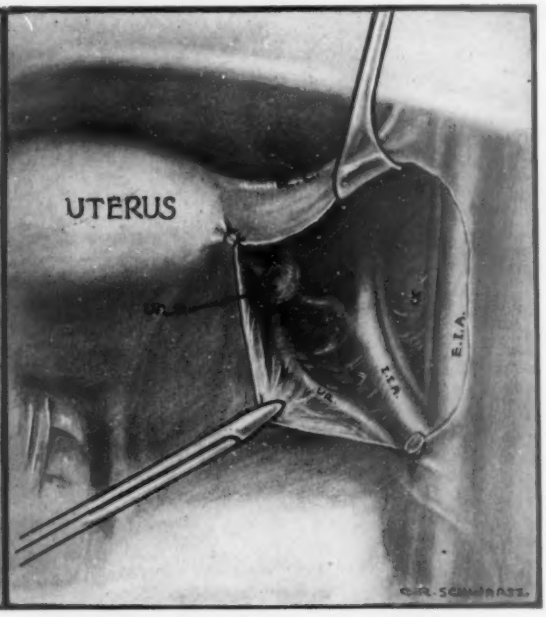

FIG. 2. Iliac lymphadenectomy. Deeper exposure to show location of enlarged ureteral gland (*UR.G.*) over the intersection of ureter and uterine artery.

A few points in the technique of this operation of iliac lymphadenectomy should be stressed. The necessity for complete intestinal relaxation in order clearly to expose the deep lateral portions of the pelvis makes spinal anesthesia the preferred narcosis. A small amount of general anesthesia was required for longer operations, but usually the time consumed was between sixty to seventy-five minutes. The tubes and ovaries were removed as a preliminary to the gland dissection since this permitted easier identification and exposure of the ureter and large vessels. Furthermore, a reduction in the uterine blood supply, and, in younger persons, the removal of hormonal influences stimulating cancer growth were a definite advantage. The exposure is certainly far better than in the operation suggested by Leveuf and Godard, in which the lymph gland area is opened after cutting across the round ligament. Their report comprises only 3 such operations.

In Figure 1 is shown the first step in the operation of iliac lymphadenectomy. The infundibulo-pelvic ligament and the tube and ovarian ligament have been ligated and cut leaving the folds of the broad ligament exposed. The iliac and obturator glands are seen as they lie pocketed in the bifurcation of the iliac vessels and along the obturator nerve, with the ureter clinging to the posterior sheath of the broad ligament. These glands can usually be better felt than seen amid the surrounding mass of fatty areolar tissue. Care is taken to avoid injury to the deeper veins and the obturator nerve. In Figure 2 is seen the location of the ureteral gland at the point of crossing between ureter and uterine vessels. The nutrient vessels are usually small and easily ligated except around the ureteral gland. Here greater care must be observed. After removing all glands and fat lying on the external iliac vessels up to the femoral ring the large open wound is closed and also compressed to prevent oozing by suturing the round ligament to the sacro-uterine of the same side. A running peritoneal stitch seals this wound. The operation is repeated on the other side.

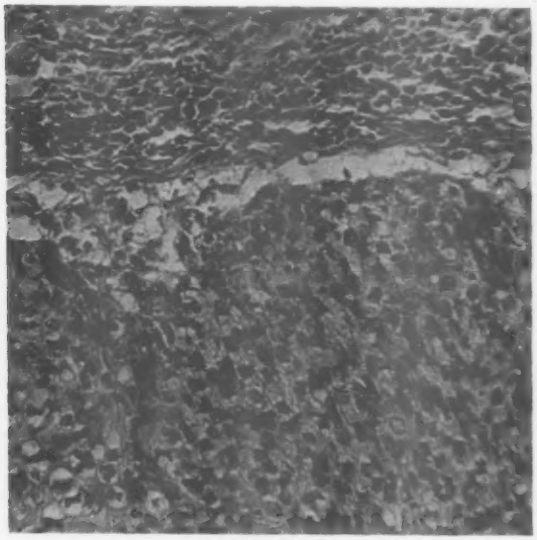

Fig. 3. Cancer metastasis in hypogastric lymph gland removed at operation October 30, 1930. Patient is still free of recurrence at present, over seven years since operation.

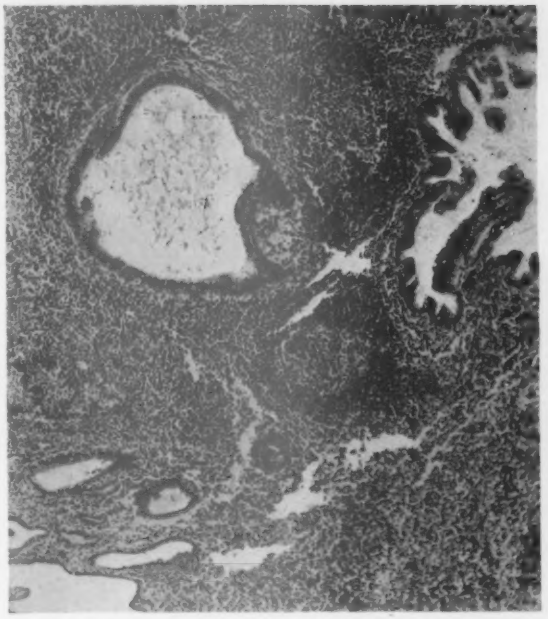

Fig. 4. Endometrium-like structure in hypogastric lymph gland, removed by iliac lymphadenectomy for squamous cell cancer of the cervix.

Microscopic study of the removed lymph glands reveals some interesting points. In Figure 3 is shown a large lymph gland

metastasis found in the first patient I operated on in October, 1930. This patient has been repeatedly examined and is now free of any recurrence over seven years. Two others of my five-year cures had

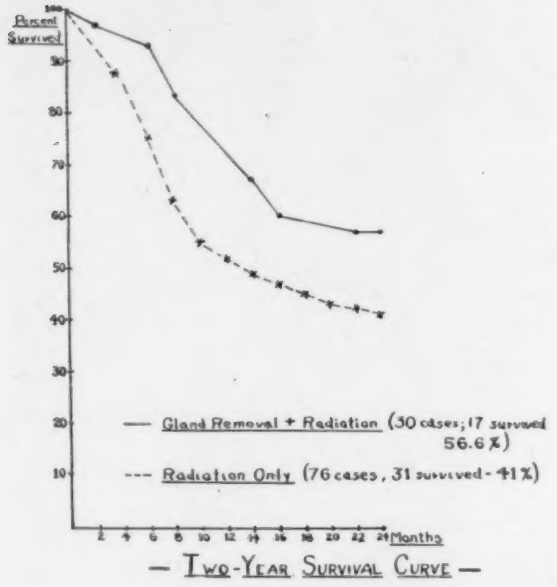
Percent Survived
Gland Removal + Radiation (30 cases; 17 survived 56.6%)
Radiation Only (76 cases, 31 survived - 41%)
Months
— Two-Year Survival Curve —

FIG. 5. Two-year survival curve, showing a surplus of 15 per cent in the cases where an iliac gland removal was added to the radiation treatment.

lymph gland metastases. A peculiar glandular hyperplasia was found in one lymph gland (Fig. 4). The cervical cancer in this patient was squamous cell. Leveuf and Godard, Wertheim, and others, call these structures metastases with epithelial metaplasia. I am unconvinced of this. They resemble endometrial implants but seem to be more common in cervical cancer. They are not included as cancer metastases in my series.

I have tried to evaluate the results of this method of combined irradiation and lymphadenectomy by comparing the survival curves of these patients with those treated by irradiation alone. The cases selected were from the same hospital, treated by the same method of irradiation (roentgen rays and radium) and from cases of the same degree of involvement (Group II). In the one series there was the additional procedure of iliac lymphadenectomy. It is seen that in this two-year survival curve (Fig. 5) 30 cases were operated on and 76 were treated by irradiation alone. The operative series (in solid lines) showed a survival of 17, or 56.6 per cent, while those only irradiated (in broken lines) showed 31 survivals, or 41 per cent, a difference of 15 per cent in favor of the cases operated upon. In Figure 6 are shown the five-year results which, although covering a smaller group, present an even more striking contrast. Ten irradiated and operated cases are compared with 35 cases treated with irradiation alone. The survival curve for the first two years is almost identical with the preceding two-year curve, a difference at the end of that time of 15 per cent. During the following three years the death rate in those not operated upon is far more rapid, so that at the end of the fifth year there is an advantage of 30 per cent in favor of those subjected to the additional procedure of iliac lymphadenectomy. There were 5 out of 10 operative patients who survived the five-year period (50 per cent), whereas out of 35 irradiated Group II cases only 7 were living after five years (20 per cent). While the

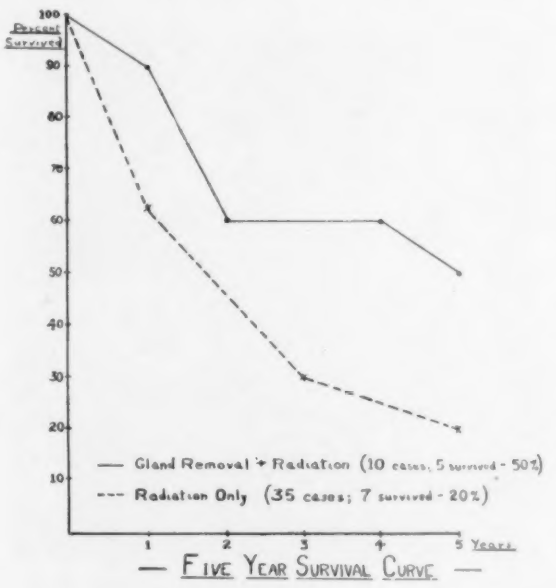
Percent Survived
Gland Removal + Radiation (10 cases; 5 survived - 50%)
Radiation Only (35 cases; 7 survived - 20%)
Years
— Five Year Survival Curve —

FIG. 6. Five-year survival curve, showing a surplus of 30 per cent in favor of the additional gland operation.

numbers are still small, it would seem that the value of the gland removal operation lies primarily in preventing to some degree those recurrences that arise between the second and the fifth year. This corresponds with our past clinical experiences in which, after complete local healing, the patient came back in two or three years with pressure pains down the thigh and a mass in the lateral region of the pelvis. This operation has been accepted for Group II cases in several large clinics and I hope that in the course of the next five years its value may be definitely established. Certainly thus far we have every reason to be satisfied with the results.

HEREDITARY CHANGES IN THE DESCENDANTS OF FEMALE MICE EXPOSED TO ROENTGEN RAYS*

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INTRODUCTION

NUMEROUS experiments have been performed to determine whether roentgen irradiation produces hereditary changes in the germ cells of animals and plants. Early workers reported sterility effects and the presence of non-viable embryos following treatment of the parents. In the first experiment performed on an adequate scale and with suitable biological material, Little and Bagg[5] found definite evidence of the production of transmissible changes. Among the descendants of their roentgen irradiated mice there appeared a number of stillborn young and one live-born individual showing absence of the top of the cranium and abnormal eyes and brain. In the light of later researches, these may be interpreted as probably due to an induced translocation, that is to say, the breaking of a chromosome through the action of the radiation and the attachment of the fragment to another chromosome, but in the state of genetic knowledge at the time interpretation was impossible. This is the first case on record of an induced change. The first proof of the high effectiveness of roentgen rays in producing mutations was furnished by the researches of Muller.[6] His investigations with the fruit fly, *Drosophila melanogaster*, have been expanded by other workers to include a large variety of plants and animals.

The changes produced may be classified under two headings. The first is *chromosome mutations* in which whole chromosomes or whole sections of chromosomes are involved. Most important of these are *simple translocations* in which a piece is broken from one chromosome and attached to another, *reciprocal translocations* in which two chromosomes exchange pieces (distinguished from crossing-over by the fact that the two chromosomes involved are not members of the same pair), *inversions* in which a segment of a chromosome is turned end for end, and *deletions* in which a portion of the chromosome is entirely lost or deleted. Chromosome mutations in favorable cases are microscopically visible. The second group consists of *gene mutations*, i.e., changes in the individual, submicroscopic hereditary unit or gene.

The hereditary behavior of reciprocal translocations is indicated in Figure 1.

Of the numerous roentgen-ray mutation studies with mammals, those with mice have given much the most significant results. This probably indicates, not that mice are in any peculiar way susceptible to the rays, but merely that large numbers of animals such as can most easily be raised with mice are necessary for the successful conduct of such studies.

When male mice are irradiated, a considerable proportion of the offspring (about one-third for a dose of 600 r) are either completely sterile or consistently produce small litters.[4,15,17] The tendency to produce small litters has been designated "semi-sterility." Evidence has been advanced indicating that it is transmitted to a proportion of the offspring, commonly one-half, other offspring being entirely normal; that the small litter size results, not from any failure to form embryos, but rather from

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the death of some of these *in utero* or at term; that the abnormality responsible for the death of those embryos which survive to the later stages is cranioschisis due to failure of the neural groove to close in the brain region; and that the basic cause is the presence of translocations induced by

With the exception of the experiment of Little and Bagg[5] cited above (in which both sexes were irradiated), all experiments in which female mammals have been irradiated have failed to give definite evidence of any induced alteration in heredity. Perhaps the most thorough researches are those of

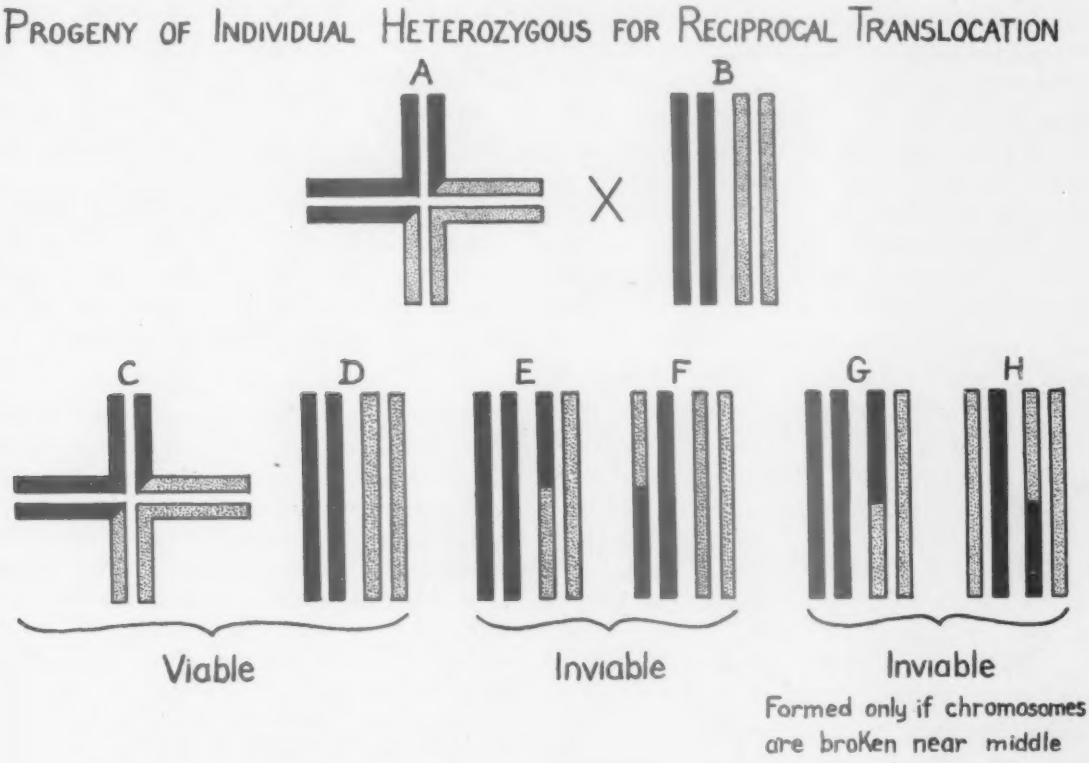

FIG. 1. Diagram showing the hereditary behavior of reciprocal translocations, based on translocations involving the second and third chromosomes of *Drosophila melanogaster* as studied by Glass, and by Dobzhansky and Sturtevant. *A*, two pairs of chromosomes that have undergone reciprocal translocation shown as paired prior to germ cell formation. The solid portions were originally one pair of chromosomes, the shaded portions a second pair. All other pairs of chromosomes are omitted in the figure. *B*, the same chromosomes in a normal individual. Matings between individuals of the types *A* and *B* give rise to individuals of the types *C*, *D*, *E*, *F*, *G*, and *H*. *C* is viable and normal in appearance, but transmits the translocation. *D* is entirely normal. *E*, *F*, *G*, and *H* are usually inviable. In mice they sometimes give rise to monsters with cranioschisis due to failure of the neural groove to close at the anterior end; more commonly, affected embryos die in early stages of development. Types *A* and *B* are produced with equal frequency, and together make up at least 50 per cent of all types.

the treatment.[17,18,19] Hertwig,[4] however, suggests an explanation in terms of a combined genetic (gene?) and physiological effect of the irradiation, at least for some of her cases.

Snell[17] failed to find evidence for the induction of gene mutations.

Dyroff,[1] Yamamoto,[20] and Murphy.[11] It is quite possible that translocations or other chromosome changes were induced in their experiments, but failed of detection because the necessary genetic tests were not employed.

In the case of humans, numerous studies

have been made of clinical cases to determine if children are affected through the preconception ovarian irradiation of the mother. In particular, we may cite the investigations of Nürnberger,[14] Goldstein,[3] Murphy,[7,8,9] Murphy and Goldstein.[12] The results of these studies are well summed up by Murphy in the statement, "Irradiation *before conception* may be followed by the birth of unhealthy or defective children. It cannot definitely be stated that such maternal treatment has a detrimental influence on the health of subsequent children." In this connection it is noteworthy, arguing from theoretical genetics and from the experiments with mice cited above, that it is usually not until the second generation following the irradiation that the genetic effects thereof become apparent. The most probable visible change in the immediate offspring of a treated female would be a change in the structure of the testes or ovaries, and this of course would not be externally visible.

MATERIAL AND METHODS

All irradiated and control females came from the MacDowell-Bagg albino strain (C strain). This strain has been inbred for about thirty-five generations by brother-sister matings and consequently is very uniform. Males were from the M strain, or in a few cases from the P strain, both inbred strains carrying recessive genes useful in testing for linkage of induced translocations in later generations.

Females to be treated were placed in a lead chamber (made from lead pipe) just large enough to hold them, with a barred opening at the front end to admit air and a window of thin aluminum over the region of the ovaries. The conditions of irradiation were as follows:

Filters: 0.50 mm. of copper, 1.00 mm. of aluminum.

20 ma.

200 kv.

Distance from target to top of lead chamber, 50 cm.

This set-up delivered 35 r per minute to a dosimeter placed beneath the aluminum window of the lead chamber.

Daily vaginal smears from each female were followed for a week or two before treatment, and continued after treatment, and the placing of a male with the female, until a vaginal plug was noted. Sterile matings were not uncommon, so observations of vaginal smears and for vaginal plugs were resumed if signs of pregnancy failed to appear.

Pregnant females were isolated in separate pens and observed, as a rule, daily, till the birth of the litter.

The fertility of the first generation offspring of the irradiated and the control females (hereinafter referred to as F_1 mice) was tested by mating to unrelated animals of a non-irradiated inbred stock.

EXPERIMENTAL FINDINGS

In a preliminary experiment, one of us (Snell, using a machine and set-up different from that described above, and one for which dosimeter readings were not available) irradiated 16 female mice with varying dosages, allowed them to mate, and killed them at twelve to thirteen days following mating. Five untreated females were likewise mated and killed to serve as controls. The results suggest quite a different situation from that noted when the male parent was irradiated. In the latter case (Snell[16]) the decrease in the average number of F_1 young per litter is related to the increase in dosage by a simple exponential formula. In the case here studied, the fall-off in fertility with increasing dosage appeared to be much more marked. The females treated with the larger doses contained a large proportion of dead embryos, apparently grossly normal, but often very loosely attached to the uterus. Quite possibly the larger doses interfered with normal implanation, either through action on the secretions of the ovary, or through direct action on the cells of the uterine wall. Whatever the explanation, the results indicated that in order to obtain viable young from irradiated females, it would be advisable to use a dose smaller than the one that is most effective in producing induced translocations in males. Young have been obtained from males irradiated with doses up to 1,200 r. Doses in the neighborhood of 600 r prove most effective. The dose finally

TABLE I

DATA CONCERNING F_1 MICE

Days from irradiation to fertile mating	3–5	6–8	9–11	12–14	15–17	18–20	21–23	24–26	27–29	Totals	Control
Number of F_1 litters	8	6	4	1	10	6	1	2	1	39	13
Total number of F_1 young	45	31	22	6	53	28	4	5	6	200	92
Mean F_1 litter size	5.6	5.2	5.5	6	5.3	4.7	4	2.5	6	5.1 ± .2	7.1 ± .6
Number of F_1 young tested	30	27	14	3	39	26	4	4	4	151	71
Colony number of F_1 young probably affected	♀ $F_1$82 ♂ $F_1$251a				♂ $F_1$111 ♂ $F_1$112 ♀ F_1 72 ♀ $F_1$194 ♀ $F_1$195 ♂ $F_1$196				♀ $F_1$74		

adopted for the irradiation of females was much less than this, being in the neighborhood of 260 r (range 240 to 280 r).

The females were irradiated in two groups. The first group gave indication of a special susceptibility of the eggs to the roentgen rays at sixteen days prior to ovulation. The second group was run to check this point. Since it gave negative results, the results from both groups are treated together in what follows.

Fifty-six strain C females were irradiated with doses ranging from 240 to 280 r and placed with M or P strain males. Eighteen of these females yielded no litters, though some of them may have aborted in the early stages of pregnancy; 37 females gave birth to a single litter each; 1 female, whose first litter was killed at birth, gave birth to two litters. The last fertile mating occurred at twenty-seven days following irradiation. Although the majority of the treated females were returned to pens with fertile males after their first litter was weaned, and kept with these males till death, none of them became pregnant again. The 38 fertile irradiated females thus produced thirty-nine litters, with a total of 200 young, an average of 5.1 ± .2 per litter. Nine control females produced thirteen litters totalling 92 young, an average of 7.1 ± .6 young per litter. These results are summarized in Table 1.

Of the 200 F_1 mice in the irradiated group, 159 were tested for sterility or semisterility by mating to unrelated mice of untreated stocks. Of the 92 F_1 mice in the control group, 71 were likewise tested. The results are summarized in Tables 1 and 11.

It will be seen that 9 F_1 individuals in the test group were probably affected, none in the control group. The nature of the effect in each case is indicated below.

♀ F_172. A daughter of ♀ F_172, mated to unrelated, untreated males, gave six litters totalling 56 young, an average of 9.3 young per litter. One of these was stillborn and abnormal. The roof of the cranium and the brain were lacking; there were no eyes, though the eye sockets were covered by skin; the floor of the brain case was greatly narrowed, particularly at the anterior end; and the basisphenoid and the basioccipital, instead of lying in the same plane, formed an upward-projecting obtuse angle. The abnormality can be classified as cranioschisis probably combined with anencephaly. There is some doubt as to the latter, because protruding brain tissue in stillborn young is often eaten by the mother. Female F_172 was probably not semisterile, as her five litters averaged 9 young each. Seventy-three offspring by two sons were all normal. The evidence available does not permit a genetic interpretation of the abnormality.

♀ F_174 and ♂ F_175. A mating of ♀ F_174 to her brother ♂ F_175 gave a litter of 11 young, one of which was abnormal, showing a skin-covered

TABLE II

TRANSMISSION OF SEMISTERILITY TO F_2 AND F_3 MICE

F_2 from $F_1$111 Stock			F_3 from $F_1$111 Stock			F_2 from $F_1$112 Stock			F_2 from $F_1$194 Stock		
Sex and Colony No. of F_2 Mice	No. of Litters	Mean Litter Size	Sex and Colony No. of F_2 Mice	No. of Litters	Mean Litter Size	Sex and Colony No. of F_2 Mice	No. of Litters	Mean Litter Size	Sex and Colony No. of F_2 Mice	No. of Litters	Mean Litter Size
(a) Probably semisterile			(a) Probably semisterile			(a) Probably semisterile			(a) Probably semisterile		
♂$F_2$132	6	2.0	♂$F_3$193	3	2.3	♂$F_2$188	1	2.0	♂$F_2$201	3	2.3
♂$F_2$73	5	2.6	♀$F_3$205	3	2.7	♂$F_2$148	11	2.2	♂$F_2$197	3	2.3
♀$F_2$95	7	2.7	♂$F_3$212	6	2.8	♂$F_2$120	8	2.2	♀$F_2$104	8	3.0
♀$F_2$72	3	3.0	♀$F_3$202	5	3.2	♂$F_2$178	4	2.2	♀F_235	7	5.0
♀$F_2$91	3	3.0	♂$F_3$233	3	3.3	♀$F_2$139	3	2.3			
♂$F_2$74	9	3.1	♂$F_3$195	4	3.5	♂$F_2$175	5	2.4	(b) Probably normal		
♂$F_2$76	4	3.2	♂$F_3$203	5	3.6	♂$F_2$176	4	2.5	♂$F_2$155	14	6.8
♂$F_2$159	6	3.5	♂$F_3$191	6	3.7	♂$F_2$147	8	2.6	♂$F_2$152	12	6.9
♀F_275	6	3.5	♂$F_3$231	5	3.6	♂$F_2$100	5	2.6	♀$F_2$181	1	7.0
♂$F_2$127	8	3.7	♂$F_3$232	3	4.0	♀$F_2$142	5	2.8	♂$F_3$200	4	7.0
♀$F_2$158	4	3.7	♂$F_3$230	5	4.2	♂$F_2$119	6	3.0	♂$F_2$151	12	7.1
♀$F_2$130	8	4.9	♀$F_3$229	4	4.7	♂$F_2$177	6	3.3	♂$F_2$184	6	7.2
			♀$F_3$194	6	5.0	♀F_297	5	3.4	♂F_236	9	7.3
(b) Probably normal						♂$F_2$150	8	3.6	♂$F_2$154	5	7.8
♂$F_2$126	7	7.1	(b) Probably normal			♀$F_2$169	4	3.7	♂$F_2$183	6	8.2
♀$F_2$131	4	7.5	♂$F_3$209	8	6.7	♀$F_2$141	5	3.8	♂$F_2$185	6	8.3
♀F_292	9	7.6	♂$F_3$208	18	6.8	♀$F_2$121	5	4.0	♂$F_2$153	7	8.7
♂F_294	10	7.8	♂$F_3$206	11	7.3	♀$F_2$103	6	4.7	♂$F_2$106	4	9.0
♀F_296	7	8.6	♂$F_3$207	5	7.4				♀$F_2$180	1	9.0
♂F_277	6	9.0	♂$F_3$192	14	8.6	(b) Probably normal			♀$F_2$105	6	9.2
♂F_293	2	10.5	♂$F_3$204	5	9.0	♂$F_2$144	20	6.6	♀$F_2$196	4	9.5
			♀$F_3$210	3	9.7	♂$F_2$146	19	6.7	♀$F_2$182	1	10.0
			♀$F_3$211	2	10.0	♂$F_2$145	12	6.8			
						♂$F_2$149	5	6.8			
						♂$F_2$164	4	7.0			
						♂$F_2$157	6	7.8			
						♀$F_2$102	5	8.8			
						♀F_299	5	9.0			
						♂$F_2$101	5	9.4			
						♀$F_2$168	4	9.7			
						♀$F_2$140	4	10.5			
						♂F_298	3	10.7			
						♀$F_2$167	3	11.0			
						♀$F_2$156	4	12.2			

hernia of brain tissue about the size of a small half pea through an approximately circular opening between the frontal bones. This individual, a male, was liveborn, and lived for five weeks, though growing more slowly than its normal sibs. Nine other litters from this mating totalled 99 young, all normal. Two litters from ♀ $F_1$74 by an unrelated, untreated male totalled 26 young, all normal; four litters from ♂$F_1$75 by unrelated, untreated females totalled 31 young, all normal. There is no evidence of semisterility in this case. The genetic interpretation is uncertain.

♀ *$F_1$82.* Female $F_1$82 mated to a male from untreated stock gave eight litters, averaging 7.9 young. One individual in the third litter, ♂$F_2$80, was abnormal, having a small papilla on the top of the head over the frontal bones. Placed with 5 different females of known fertility, ♂$F_2$80 failed to produce young. He was killed at eight months of age. Observation of the contents of the vasa deferentia showed

active sperm. The skull contained an extra bone between the frontal bones (Fig. 2). Besides ♂$F_2$80, 18 offspring of ♀ $F_1$82 were tested. All gave litters of normal size. The genetic interpretation of this case is uncertain.

♂F1111. Male $F_1$111, mated to females from untreated stock, gave twelve litters averaging 2.7 young. He was therefore clearly semisterile. Of 19 tested offspring, 12 were likewise semisterile, 7 probably normal (Table II, F_2 from $F_1$111-stock). Likewise 13 of 21 F_3 individuals by a semisterile F_2♂ and females from untreated stock were semisterile. If semisterility be due to the segregation of a translocation, the expected ratio of semisteriles to normals from a mating of this type is 1:1. The excess of semisteriles in this case may be due to chance, or may indicate that something more than a single simple or reciprocal translocation is involved.

♂F1112. Male $F_1$112 was a brother of $F_1$111. Mated to females from untreated stock he gave ten litters averaging 3.1 young. The semisterility was transmitted to the second generation, the ratio of 18 semisterile to 14 normal F_2 (Table II) indicating that it was caused by a translocation. ♂$F_1$111 and ♂$F_1$112 had no other brothers, but one sister, a normal.

♀F1194. Female $F_1$194 mated to a male from untreated stock gave five litters averaging 4.6 young. Of 20 tested offspring from this mating, 4 were semisterile like the mother. The ratio in this case cannot be explained without further analysis. One possibility is that $F_1$194 carried two translocations causing a relatively slight reduction in litter size when acting singly, a considerable reduction when combined.

♀F1195. Female $F_1$195 was a sister of ♀ $F_1$194. She was conspicuously small at one month of age and remained small throughout life. She was placed with two different males but failed to give any litters. She died at seven months of age, autopsy revealing a lymphoblastoma of sarcoma type in the intestinal lymph nodes, spleen and thymus. The ovaries had been invaded by the lymphoblastoma. They showed egg tubes and a few primordial follicles, but no mature follicles.

♂F1196. ♂$F_1$196 was a brother of ♀ $F_1$194 and ♀ $F_1$195. He was placed with six different females of known fertility but failed to produce young. He was killed at seven months of age and the genital tract examined. There were no sperm in the vasa deferentia. The testes were small. Sections showed interstitial cells and seminiferous tubules to be present, the latter containing spermatogonia and spermatocytes but no spermatids or spermatozoa. Degenerative changes were occurring in the seminiferous epithelium, evidenced by hydrotic degeneration and vacuolization, fragmentation and pycnosis of nuclei, or complete necrosis. There were some mitoses.

Fig. 2. Skull of ♂$F_2$80, showing extra bone inserted between the frontals.

♂F1251a. Male $F_1$251a, one of a litter of 6, was sterile, failing to produce young by any of five different females of known fertility. He was killed at seven months of age and the genital tract examined. Well developed vasa deferentia and epididymides were present, but no testes. Serial sections confirmed the observation that testes were completely absent.

Abnormal Embryo from Irradiated Female in the Preliminary Experiment. Female Alb 9 was irradiated, mated to a normal male one and a half days after irradiation, and killed twelve days after mating. In the uterus were found 10 embryos, 9 living and 1 that had died at an early stage. Of the living embryos, 8 were perfectly normal, the remaining 1 was grossly abnormal in the brain region due to failure of the neural groove to close. The abnormality was indistinguishable from abnormalities resulting from the unbalanced chromosome recombinations of translocations. However, it cannot have

been due to a translocation, because translocations do not cause unbalanced chromosome recombinations until the second generation following irradiation. It may have been due to an induced deletion. This would give chromosomal unbalance in the first generation. Moreover, it has been shown that roentgen irradiation produces deletions in a variety of plants and animals. It is noteworthy that among hundreds of embryos from untreated stock, we have never observed this type of abnormality.

SUMMARY AND CONCLUSIONS

1. Female mice irradiated with 240 to 280 roentgens may give fertile matings for at least three or four weeks following treatment. Later they are entirely sterile. The occurrence of sterility is in accord with the histological observations of Murray[13] who states that "structural 'sterility' is produced in ovaries exposed to 150 r or more, the primary follicles being absent after two days, and all follicular elements absent by the forty-third day after irradiation." Genther,[2] who irradiated female guinea pigs with doses up to 2,160 r, obtained fertile matings up to at least ten weeks following treatment. It should be noted in this connection that guinea pigs are probably much more resistant to irradiation than mice (see Snell,[16] p. 433).

2. When the mother is irradiated with a dose of 240–280 r, the mean litter size is reduced from the figure of $7.1 \pm .6$ found for control animals, to $5.1 \pm .2$. A reduction in F_1 litter size has likewise been noted by Murphy[10,11] in experiments with rats. Irradiated male mice show approximately the same reduction in litter size for the same dose.[16]

3. For larger doses, there is some evidence that the fertility falls off more rapidly for irradiated female mice than for irradiated male mice. This may be due to an effect of the irradiation on the capacity of the ovary to form corpora lutea, or on the cells of the uterine wall, interfering with the normal course of pregnancy, rather than to an effect on the eggs themselves.

4. Of 151 tested F_1 animals from irradiated mothers (dose 240–280 r), 9, or 6 per cent, gave rise to lines probably carrying altered heredity.

Of these 9 lines, 3 produced only one abnormal mouse each. Numerous other descendants were entirely normal. In one case the abnormal individual was stillborn, lacking brain and cranial roof; in another case there was a hernia of brain tissue through a hole in the cranial roof; in the third case there was a papilla on top of the head and an extra bone in the cranial roof between the frontals. The genetic interpretation of these cases is uncertain.

Three other affected F_1 mice were semisterile, consistently producing small litters. The semisterility was transmitted to later generations, and was probably the result of translocations induced by the treatment.

The last three affected F_1 mice (1 female and 2 males) were completely sterile. Sections of gonads showed abnormal ovaries in the case of the female, abnormal testes lacking spermatids and spermatozoa in the case of one male, and complete absence of testes in the case of the second male. Hertwig[4] has described similar F_1 individuals following irradiation of the father.

5. All of the 71 tested F_1 animals from control mothers proved entirely normal.

We wish to thank Dr. C. C. Little for his continued aid and encouragement during the course of this investigation.

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MEASUREMENT OF SUPERVOLTAGE X-RAYS WITH THE FREE-AIR IONIZATION CHAMBER*

By LAURISTON S. TAYLOR, GEORGE SINGER, AND ARVID L. CHARLTON

I. INTRODUCTION

THE internationally accepted definition of the unit of x-ray quantity has from the first been based upon the ionization produced in a unit volume of unrestricted air [1].[1] The original definition was, in fact, a statement of the physical requirements for reproducing a unit in terms of the ionization in a free-air ionization chamber. This unit has served its purpose very well for the x-ray voltages in use up to within the past 3 or 4 years. However, with excitations in excess of 200 kv., various mechanical and physical difficulties have appeared to limit the applicability of the definition, as well as of the free-air ionization chamber used to determine it.

Consequently, there has been an increasing trend toward the use of thimble chambers for the fundamental realization of the roentgen. The theoretical as well as experimental evidence favoring this trend appears to be reasonably sound, particularly as regards theory. Experimentally the problem has presented great difficulties which, in the hands of a few experimenters, seem to have been adequately overcome. There remains, even for them, the problem of definitely and irrefutably tying together the thimble-chamber measurements in the supervoltage region with free-air measurements in the high-voltage region. The thimble-chamber measurements appear to be self-consistent, but it is definitely desirable to check them by a wholly independent means and at the same time correlate them with the free-air measurements at the lower voltages.

In order to validate thimble-chamber measurements in the supervoltage region it has been necessary to redefine the roentgen. This was done at the Fifth International Congress of Radiology [2] as follows: "The roentgen shall be the quantity of X or gamma radiation such that the associated corpuscular emission per 0.001 293 gram of air produces, in air, ions carrying 1 e. s. u. of quantity of electricity of either sign." It is not proposed to discuss this definition in its relation to thimble chambers; it has already been ably done by Mayneord [3, 4], Lauritsen [5, 6, 7], Gray [8, 9, 10], Laurence [11], Failla [14], and others. In connection with the use of free-air chambers,[2] however, two points of prime importance must be mentioned. First, the physical magnitude of the unit is exactly the same as in the older definition for excitations below about 200 kv. (peak). Secondly, the new definition removes the question of inclusion or exclusion of scattered radiation in free-air measurements made in the supervoltage region—a question which had been troubling the American x-ray standardization committees for some years [12]. The new definition therefore makes it possible and desirable to extend the useful range of the free-air chamber up to indefinitely high voltages, provided the design characteristics can be adequately worked out in conformity with the definition. It is the purpose of this paper to describe equipment designed for the investigation of these problems and to report measurements obtained in the 200- to 400-kv. range, designed to test the conditions essential for realizing the definition of the roentgen. It should, of course, be emphasized that the particular design employed in this study is not necessary in all cases, but was so chosen as to yield the

[1] Numbers in brackets refer to the citations listed at the end of this paper.

[2] "Free-air" ionization chambers may be classed roughly as those in which chamber walls contribute nothing to the measurement. This may, of course, include chambers operated above atmospheric pressure.

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937. Reprinted from the *National Bureau of Standards Journal of Research.*

design factors for any particular voltage range desired.

We will review very briefly the several investigations of free-air ionization chambers for the measurement of supervoltage or gamma radiations, and point out what appears to us to be the limitations of each of these several studies insofar as relates to x-ray measurements.

The first free-air chamber for extra-hard radiations was constructed by Failla [13] in 1931. This had a maximum plate separation of about 1 m. and a length of about 1.5 m. Field correction was provided by means of the guard-wire principle such as developed for our lower-voltage chambers [15]. Because of size limitations this chamber did not prove successful in the measurement of gamma rays. Failla was also unable to use it with x-ray voltages above 200 kv. since the available treatment room was too small.

Mayneord [16] and his co-workers (1934) constructed a parallel-plate ionization chamber having a maximum plate separation of 20 cm. and plate length of 50 cm. For this a field correction was found unnecessary. Their results indicated that a plate separation of 20 cm. was sufficient for x-ray potentials up to 400 kv., and apparently also for gamma rays. However, as the measurements with this chamber showed marked divergences from the thimble-chamber measurements above 250 kv. they discarded the parallel-plate chamber as a primary standard. They gave insufficient distance between limiting diaphragm and collector as one of the main design limitations affecting the attainment of radiation equilibrium in the ionized volume.

Lauritsen [5] used a parallel-plate chamber for voltages up to 900 kv. With a plate separation of 30 cm., radiation equilibrium was apparently obtained by placing the chamber at a considerable distance from the limiting diaphragm and using a very narrow beam of radiation. No direct evidence for the adequacy of the 30-cm. plate spacing was given. In a personal communication he showed a Wilson cloud-expansion photograph of a narrow 700-kv. x-ray beam wherein the tracks appeared to be limited to a region about 10 cm. on both sides of the beam. No data were given tying directly his supervoltage measurements to high- or low-voltage measurements.

Jaeger [17] has reported on the use of the PTR Fasskammer at voltages up to 500 kv., and shows perfect agreement with his "Universalkammer" for x-ray voltages from 10 to 500 kv. His free-air chamber is 25 cm. in diameter, with the collecting electrode parallel to and about 4 cm. from the axis and the collimated x-ray beam. Using lining sleeves of different diameter placed in this chamber, he apparently proves its size to be adequate. This conclusion is very difficult to reconcile with our finding that a 12-cm. plate spacing is just barely sufficient for the measurement of 180-kv. x-rays.

Kaye and Binks [18, 19] have described a large free-air ionization chamber also employing the guarded-field principle and having a plate spacing of some 3 m., which they used for measuring gamma rays. They have not reported any measurements with x-rays.

Of these various studies, Mayneord's [16] and Jaeger's [17] appear to be the most complete and yet their essential results are contradictory. We have endeavored therefore to set up an experimental arrangement which permits the overlapping of the conditions of their investigations.

II. HIGH-VOLTAGE EQUIPMENT AND X-RAY TUBE

1. General Requirements

For the investigation outlined above, as well as to provide suitable equipment for future standardization work, it seemed advisable to construct a special tube and voltage-rectifying system containing certain features conducive to the elimination of some of the uncertainties present in earlier work.

The principle requirements were: (1) A small and steady focal spot, (2) a very steady tube voltage and current, (3) a reasonably small ripplage, (4) a minimum of filtration between the target face and ionization chamber, and (5) as large a distance between target and chamber as might be necessary.

2. *Rectifier Circuit*

The electric circuit shown in Figure 1 is a simple cascade of four half-wave rectifiers

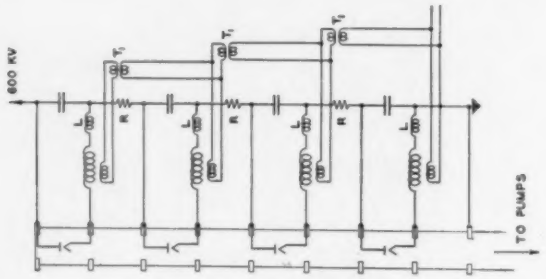

FIG. 1. Schematic diagram of 600-kv. d-c. rectifier system.

designed to give 150 kv. (constant) each. Successive units above the first were supplied through 1:1 insulation transformers (T_1), of the toroidal type having only oil insulation. Each unit was connected to its neighbor through 0.5-megohm (Glo-bar) noninductive resistors (R). The main transformers were isolated from the remainder of the circuit by small radio-frequency chokes (L), each made up of 2 lb. of size 6 AWG copper wire wound on a 2-in. Bakelite tube.

Each 150-kv. unit was placed on a wood frame supported on porcelain insulators.

Galvanized-iron "down spouting" was used for most of the conductors above 150 kv. Otherwise, little precaution was made for the avoidance of corona. Mutual shielding of many of the components apparently helped because at 400 kv., corona was neither excessive nor troublesome.

The filaments of the four rectifiers were supplied by four 1:1, 15-v. insulation transformers ($T2$) connected in series and resting atop the main transformers ($T3$) as shown in Figure 2. The rectifier tubes were made for continuous evacuation by a single apiezon oil-diffusion pump system

FIG. 2. Rectifier system and X-ray tube, looking down from one corner of the room.

[20]. Tubes of 8-in. Pyrex glass 40 in. long served as the envelope for each rectifier, which was designed for a maximum inverse voltage of 300 kv. Each electrode consisted of a 4-in. brass tube ending with a $\frac{1}{2}$-in. diameter reentrant steel beading. The filaments (F, Fig. 3) made up of 134 mm. of 15-mil tungsten, were each bent in two open loops toward the anode but not extending beyond the plane of the end of the cathode. Operating characteristics showed a space current of about 20 ma. at 1,000 v., for a filament current of 10.7 amp. The filaments could be readily removed for replacement, by removing a waxed-on cover and reaching through the anode from the top of the tube. One filament lead was fastened to the electrode and the other to a self-winding reel (R) at the bottom of the manifold.

3. *Pumping System*

The pumping system consisted of two 4-in. "fine" apiezon oil pumps feeding into a third "coarse" pump and all backed up by a Cenco Hypervac-20 pump. Baffles between the fine pumps and the glass system consisted of alternate copper rings (C) and disks, all soldered together and water cooled (Fig. 3). Although the glass above these baffles shows a pronounced yellowing, the occasional gas discharges in the tube show a definite absence of oil vapor. When first assembled no electrodes of any sort were placed in the 4-in. tubes connecting the rectifiers. With this arrangement the long mean free path was conducive to electrical breakdown and limited the over-all voltage to about 200 kv., at which point gas discharge occurred throughout the connecting tubes. This discharge condition has apparently been completely eliminated by placing in each tube, two brass electrodes (E) of thin tubing 2 in. in diameter and 3 in. long (Figs. 2 and 3). These electrodes were connected, through holes drilled in the glass tubing, to small outside points (P) which, through field pick-up, allowed the rings to assume their proper potential. Toroids (T_1 and T_2) inside and outside the connecting tubes at the ends protected the seals from puncture in case of a heavy discharge. The only puncture experienced was opposite the filament of one rectifier where there was a large air-bubble flaw in the glass envelope.

A pirani gage in the forepump line served as an indicator for the pumping speed. An

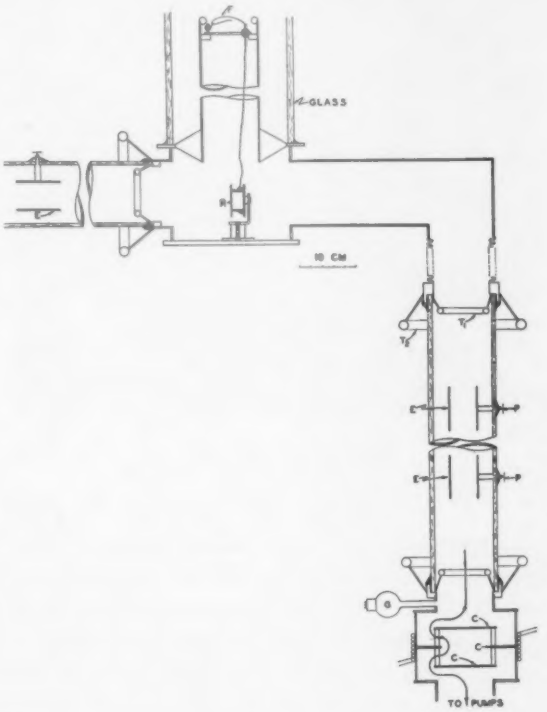

Fig. 3. Cross sections through the pump baffles and the manifold of the first rectifier tube.

ionization gage (G) located immediately above the cold baffle on one pump gave a continuous indication of the working vacuum. A second ionization gage at the base of the last rectifier proved very useful in hunting leaks. All the gage meters and controls (as well as a similar set on the x-ray tube) were located on a single panel (A) in the control room (Fig. 10), and were invaluable for studying the operation characteristics of the equipment. The working vacuum was about 3×10^{-6} mm. of mercury, and with the system shut off the pumps for 6 weeks the vacuum remained at a value of 10^{-3} mm. or better (the limit of reading the pirani gage).

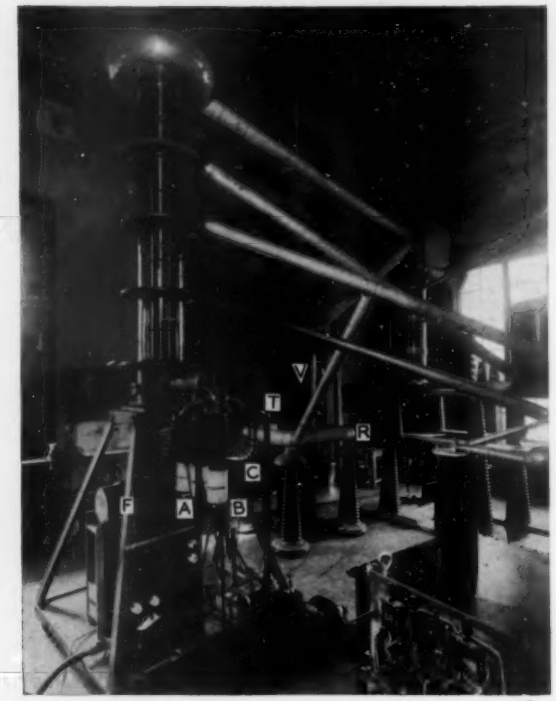

FIG. 4. X-ray tube and voltmeter (*V*).

4. X-ray Tube

It was not desired to do any unnecessary development work in the construction of our x-ray tube, so we have followed as closely as possible the design used so successfully at a million volts for nuclear physics investigations at the Department of Terrestrial Magnetism, Carnegie Institution [21].

The tube is designed for 600 kv. and consists of four sections of Pyrex-glass cylinders 12 in. in diameter by 18 in. long (Fig. 4). The electrodes were 5 in. in diameter with reentrant rolled-steel ends. Adjacent accelerating tubes were separated by a $\frac{1}{2}$-in. gap. Following Tuve [21], these electrodes were very accurately aligned during assembly by means of a long mandrel. The glass cylinders and electrodes were assembled on the floor and held in place with tie rods while the wax (pizein) joints were made. The resulting unit was then lifted into place atop the pump manifold, the tie rods being kept taut until after the tube was evacuated. They were always replaced before letting air into the system. While this procedure caused a little more trouble than with direct assembly (as first tried), it eliminated troublesome cracking of the seals from unavoidable strains.

The pumping system for the x-ray tube is somewhat faster than that used, for the rectifiers, since it was possible here to eliminate some of the long delivery tubes. The arrangement of the two fine pumps (*A*) and one coarse pump (*B*) is shown in Figure 4. The use of toilet bends (*C*), sink traps (*T*), etc., eliminated many soldered joints, as is evident from the figure. All pump connections were made with the rubber gasket seals described by Rose [39]. The pressure gages duplicated those of the rectifier system and were read at the same panels.

All operating components of both tube and rectifier were protected by an electrical interlock system to prevent errors in operation. This insured the following starting order: (1) Forepump, (2) water supply, (3) pump heaters, and (4) transformer voltage. A failure of any one would cut off all higher components and necessitate manual resetting.

(*a*) *Filament.* The filament construction is essentially of the cup focusing type shown in Figure 5. Provision is made for complete adjustment while the tube is in operation. The main filament housing (*A*) is made of thin steel tubing, $2\frac{1}{2}$ in. in diameter, extending down nearly to the center of the first glass section. Facing the filament cup is the first accelerating electrode (*B*), a flared steel tube of about the same diameter. The filament is supported on a Lavite bushing (*L*), which may be centered by means of the setscrews (*C*). Filament leads are insulated from the main housing to permit the use of biasing potentials if necessary. Vertical adjustment of the filament assembly of about 1 cm. is effected with an external pulley (*P*), the displacement being provided for by a Sylphon bellows (S_1). A lateral adjustment up to 1 cm. from the center in any direction is effected with a double ball-bearing eccentric, as described by Tuve [22], the seal being

secured with the Sylphon bellows (S_2).

The total distance from filament to target is about 8 ft. and within this path appreciable deflection of the cathode beam may be produced by the earth's magnetic field. This becomes very troublesome at the lower voltages. It was eliminated by lining the accelerating tubes with a double layer of 0.014-in. heat-treated Chrome Permalloy.

(*b*) *Target.* The target construction is shown in Figure 6. The most essential feature is its complete insulation by means of a glass gasket (G) to permit the use of a milliammeter in the ground circuit. The target (T) is of lead, electroplated on copper and mounted at the bottom of a brass tube $\frac{1}{8}$-in. thick and 5-in. in diameter in the manner described by Folsom [23]. At the point of emergence (W_1) of the x-ray beam, this tube was milled down to a uniform thickness of about 1/32 in. Surrounding the entire target tube is a 6-in. water jacket. This is provided with a reentrant window (W_2) (opposite the target window W_1) covered with 1/64-in. brass and extending in so as to nearly touch W_1. Thus the total inherent filtration of the tube consists of 3/64 inch of brass plus about 2 mm. of water.

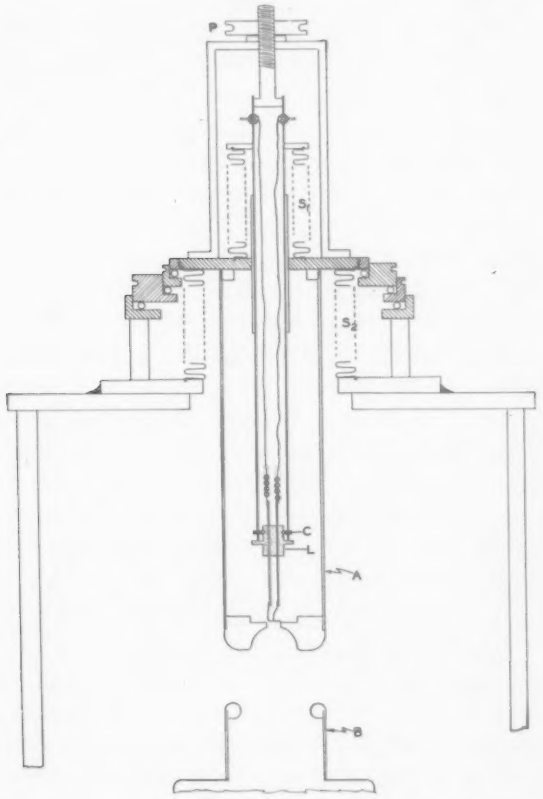

Fig. 5. Filament assembly.

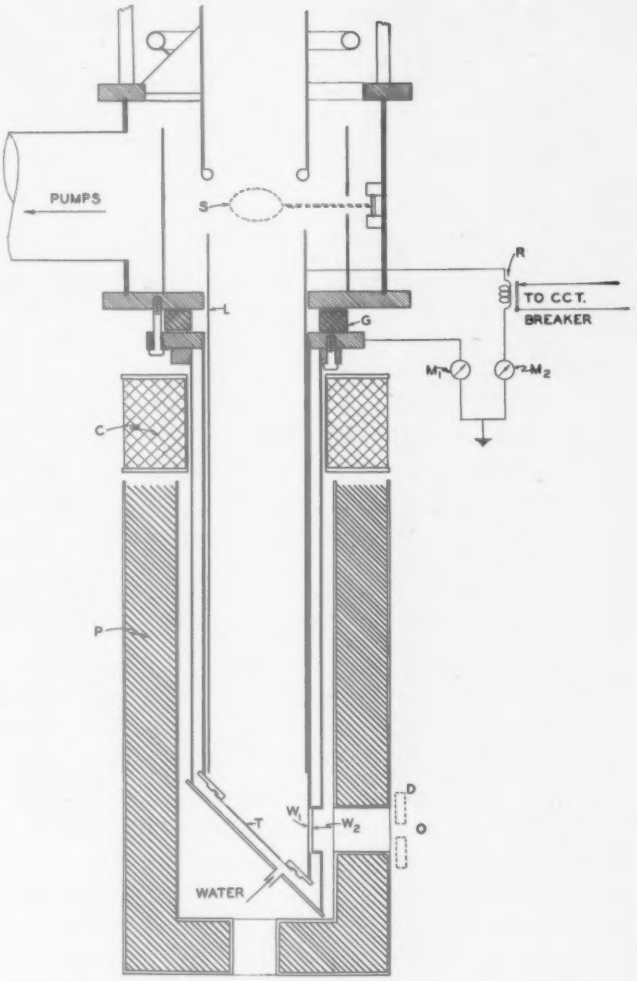

Fig. 6. Cross section through the earthed end of the X-ray tube, showing target details, focusing coil, etc.

Extending down into the target tube, and spaced $\frac{1}{8}$ in. from it, is a thin steel tube (L), which is insulated from both ground and the target. This shield tube is connected with the control room and serves three purposes: (1) It prevents the bulk of the scattered electrons from striking the target tube, so that the milliammeter (M_1) gives very nearly the true target current;

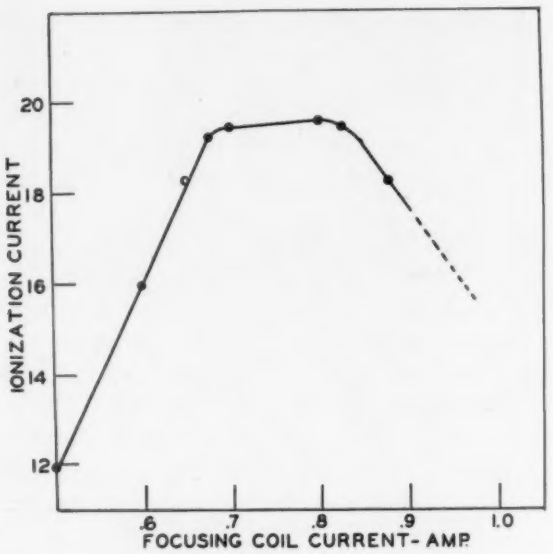

FIG. 7. Effect of focusing coil current on the radiation leaving the tube through a small diaphragm.

(2) it permits the remote reading of the current to the shield and thus allows adjustment of the focusing conditions to obtain the optimum ratio of M_1 to M_2; and (3) it operates through a sensitive relay (R) to open the circuit-breakers in the transformer circuit in case of a general gassy condition of the tube. This last result is brought about by the fact that the presence of a general "gassy" condition throughout the tube defocuses the electron beam, causing it to strike the shield and pass a releasing current through the relay circuit. This action was found to be very positive and quick, making it virtually impossible to overload the tube and destroy the target.

The target was surrounded by a double-walled iron jacket filled with 1.15-mm. lead shot (P) to a thickness of $2\frac{1}{2}$ in. in all directions, except for the two 2-in. openings shown. This effectively restricted the radiation to a narrow beam and also greatly simplified the protection problem in the x-ray tube room. An electromagnetically operated lead shutter was placed adjacent to the horizontal opening (O).

(*c*) *Focusing.* It was desired to have a reasonably small and uniform focal spot which is effectively a point source for a distance of 2 m. or more. Direct focusing from the filament cup gave a focal spot 5 to 7 cm. in diameter with a greater concentration of the electrons near the periphery. To reduce and control the size of the focal spot a focusing coil (C) was used [24]. This consisted of 4,500 turns of size 18 AWG copper wire wound on an insulated spool $2\frac{3}{4}$ in. deep and $3\frac{3}{4}$ in. along the axis. A focal spot of 2 cm. or less was readily obtainable with a current of about 0.7 amp. through the coil, the size remaining nearly constant over the voltage range of 200 to 400 kv. The current was held constant by means of an ordinary hydrogen-filled ballast lamp.

Central alignment of the beam was determined by means of a fused-quartz screen (S) that could be swung in and out of the beam through a rotary Sylphon joint and observed through a glass side window while the tube was in operation. Any necessary focusing adjustment was obtained with the double eccentric-filament adjustment described above and operated by strings from without the x-ray tube room.

The size of the focal spot was determined within the desired limits by limiting the beam with a 3-cm. diaphragm (D) located near the target, and then measuring the x-ray output with an ionization chamber some 3 m. away. Figure 7 gives a typical curve of the ionization current as a function of the current in the focusing coil. The flat peak shows that the focal spot did not overlap the temporary diaphragm and hence was of somewhat less diameter. Numerous pin-hole photographs verified these conditions and also showed a negligible amount of off-focus radiation. For normal operation a focusing-coil current at the peak of the curve was employed.

(*d*) *Distribution of Current in the X-ray Tube.* Simultaneous measurements of the target current, shield current, and current input to the high side of the tube gave a further check on the completeness of the focusing. In all cases the sum of the target and shield currents equalled the total input current within the limits of accuracy of the

meter readings. Also the target current bore a very nearly constant ratio of about 4:1 to the shield current for all voltages and tube currents used. To test for secondary radiation arising from scattered electrons striking the ends of the accelerating tubes, a pin-hole x-ray exposure of the entire tube was made; but an hour's exposure failed to reveal any image on the film.

5. *Voltage Control and Measurement*

Input voltage for the main transformers is supplied by a 25-kva. 60-cycle generator driven by a 40-hp. synchronous motor. The generator voltage was applied directly to the transformers with essentially no resistance in the line. Voltage was regulated through field rheostats located in the control room, and adjustable in steps as small as .02 ohm out of a total of about 50 ohms.

Output voltage was measured directly at the x-ray tube terminal with a 600-kv. resistance voltmeter (V), as described by Tuve [25] (Fig. 4). The resistance elements and corona shields are contained in a vertical Bakelite tube sealed to prevent the entrance of moisture. To assist in obtaining a uniform potential gradient along the Bakelite tube, a potential ring (R) is placed about its center and connected to the midpoint of the voltage cascade.

The resistance was calibrated under full working conditions against our standard 200-kv. shielded resistance voltmeter [26], which has an over-all accuracy of $\pm\frac{1}{4}$ per cent or better. To do this, the 600-kv. resistor was tapped off at intervals corresponding to 200 kv., and compared directly with the standard up to that voltage. Repeated checks have shown the resistor to be reliable within the desired limits of accuracy ($\pm\frac{1}{3}$ per cent).

6. *Tube Current Control*

The x-ray tube filament is heated with storage batteries located in a corona shield atop the last voltage cascade. A coarse hand-operated rheostat gives a preliminary current setting. Fine control is effected by two remotely operated motor-driven rheostats of which one gives a continuous adjustment over a range of about 0.1 ohm, and the other an adjustment over a range of 0.8 ohm in 25 steps. Readings of the tube current were made with a milliammeter (M_1) (Fig. 6). For control purposes a galvanometer with a displaced zero is used which renders the current easily controllable within 1 mm. in about 1,000 mm.

Occasional variations of 1 or 2 per cent in output were noted in spite of apparently steady tube current and voltage. These changes usually took place after a slight gassing or other disturbance and were no doubt caused by a slight change in the focal spot.

To eliminate this a multiplate control ionization chamber (F, Fig. 4) was placed in the beam immediately next to the shutter. The tube current was adjusted to hold the control ionization current steady at a given value of the tube voltage. By this means it is possible to hold the radiation output constant within $\pm\frac{1}{4}$ per cent over the period of a whole day. It is observed that, using this method of control, the target current does not depart from its steady value by more than 1 or 2 per cent.

III. STANDARD FREE-AIR IONIZATION CHAMBER

After reviewing the investigations outlined in the introduction, it was felt that no one of them offered the best solution to the problem of establishing a free-air standard x-ray ionization chamber. One of the principal difficulties was judged to be the inadequacy of the methods of comparison with accepted standards in other voltage ranges.

1. *Pressure Chamber*

It was decided to construct a chamber to operate under a moderate air pressure, thereby reducing operating dimensions to practicable magnitudes. The need was a single ionization chamber capable of measuring x-rays in roentgens, under the following conditions: (1) At elevated pressures,

x-rays from 200 kv. upward; (2) at atmospheric pressure, x-rays from 300 kv. downward; and (3) at such plate separations that field correction is unnecessary. It was also necessary to be able to determine air absorption corrections under all operating conditions.

The completed ionization chamber consists of a steel pressure cylinder 30 in. in diameter and 7 ft. long (inside). The rear end is completely removable (Figs. 8 and 9). Air is pumped in through a calcium chloride drier, and in addition several trays of drier are kept in the cylinder. Temperature within the chamber is measured with a thermometer fastened to the electrode assembly and read through a thick glass window at the rear.

The pressure is read and controlled from a multiple mercury manometer (*B*), as described by Meyers and Jessup [27], located in the control room (Fig. 10). The manometer tubes are of carefully selected Pyrex glass; and successive mercury columns are hydrostatically coupled with thoroughly outgassed distilled water. Each mercury column height is determined by means of a hairline ruled on a glass slider moving on a meter bar. Mirrors behind the columns prevent parallax. Settings can be read within ± 0.1 mm., making a possible over-all error on all eight columns of ± 0.8 mm., or about 1.5 mm. maximum. At 1 atm this amounts to a maximum error of very close to 0.1 per cent, which is closer than warranted by other experimental inaccuracies present.

The negative pressure effect of the water column is automatically obtained with each mercury column reading, excepting the two end columns. The end columns terminate in the center of heavy glass bulbs contained in brass protective shields (*C*) and having a cross-sectional area about 250 times that of the manometer tubing. Consequently for a maximum motion of one water column of 50 cm. the change of the end water level will be only 0.2 mm., giving a difference between the levels in the two bulbs of 0.4 mm. of water or 0.03 mm. in mercury, which can be entirely neglected. Temperature-density corrections for the water and

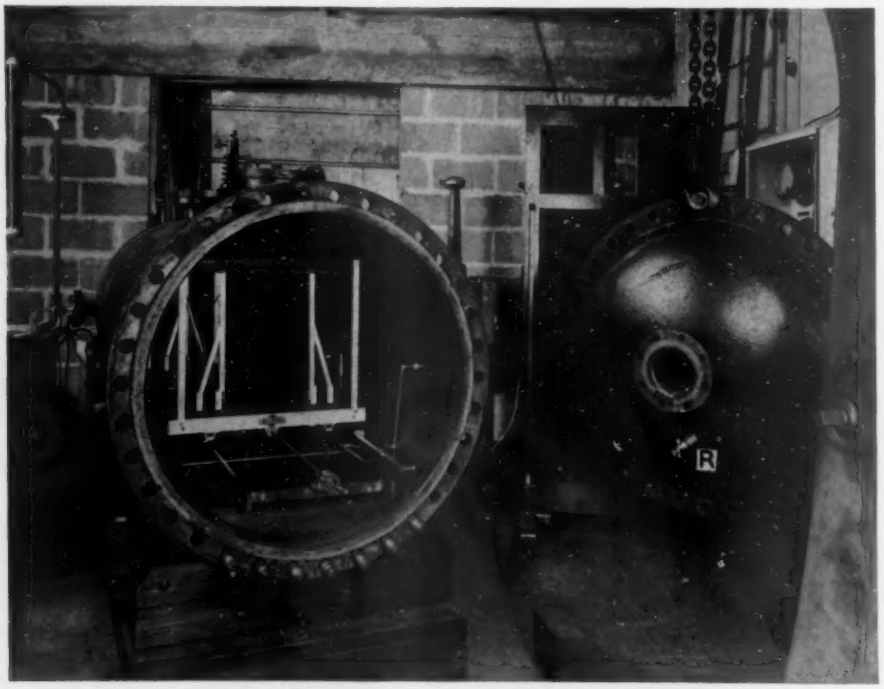

FIG. 8. Pressure ionization chamber with rear end removed.

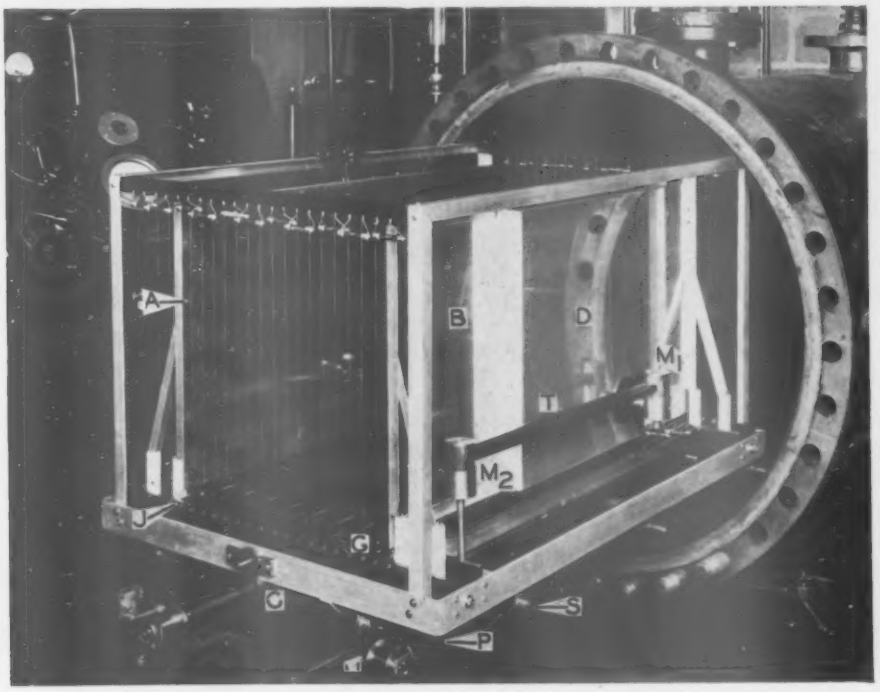

Fig. 9. Ionization chamber electrode system drawn out of rear of pressure chamber.

mercury are small for ordinary temperature changes and may usually be neglected.

For the calibration of the meter bar and for control purposes a vertical cathetometer is employed. This is easy on the eyes and permits a pressure control within 0.05 mm. of mercury on a single column.

2. *Electrode System*

The electrode system is shown in Figure 9 in which the entire assembly is pulled partially out of the rear of the chamber. The high-potential plate (*A*) and collector plate (plus guards) (*B*) are mounted on cross slides. By means of a pinion and rack (not visible) driven by the gear train (*C*) the two sets of plates may be moved smoothly toward or away from each other. The motion is transmitted to the lower gear through a sliding collar on a square shaft extending the length of the track and this in turn through a rotary Sylphon seal (*R*) in the rear of the chamber.

The over-all length of the plates is about 750 mm.; the effective length of the collector (including air gap) is 254.0 mm., and each guard plate is about 25 cm. wide. The minimum plate separation is 7.2 cm.,

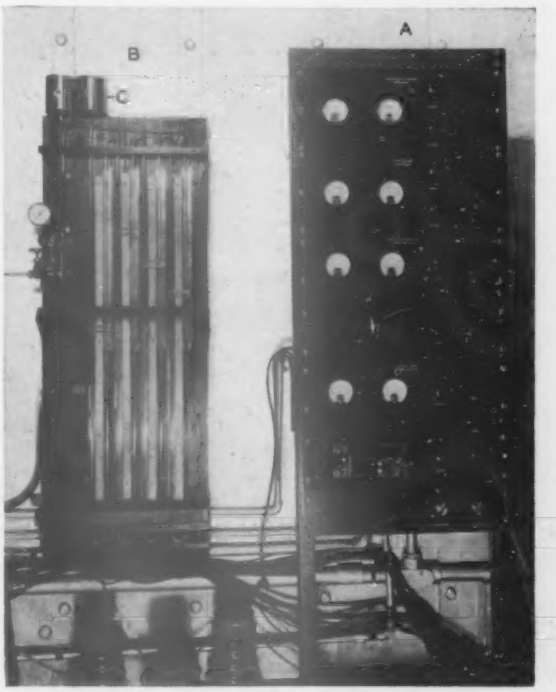

Fig. 10. Details of the multiple tube manometer and vacuum gauge panel.

and the maximum, 38 cm. The height of the collector being about 35 cm. a plate separation greater than 35 cm. is never ordinarily used since to do so would cause a loss of some of the ions under conditions where full plate separation is necessary to their full utilization.

In accordance with previous analyses [28, 29], a guard plate width of 25 cm., will permit the use of a plate separation of only 16 to 18 cm. without introducing field distortion at the edges of the collector. For greater separations therefore it is necessary to resort to the method of guarding developed in this laboratory [30, 31] for low-voltage ionization chambers.

3. *Field Correction*

In this case aluminum guard wires 0.4 mm. in diameter and 2 cm. apart were extended completely around the ionization volume of the chamber except for the small gap (*G*) near the lower corners to permit the displacement of the plates. The potential of these guard wires was uniformly distributed by insertion of a series of 2-megohm metallized resistors some of which may be seen across the top Bakelite spreader.

To insure full field correction it is important that the potential of the guard wires be uniformly graded between that of the high-potential plate and the grounded guard plate. Therefore, for small plate separations, only those guard wires falling between the plates are charged. For this purpose the high potential is applied directly to the collector plate and from there to the guard wires by means of the sliding contact (*J*). Similarly, the ground is applied directly to the guard plates and to the other end of the guard wires by means of a like contact. These two sliding contacts also serve to tie in the set of guard wires extending along the bottom of the chamber which otherwise would be isolated.

Since it was planned to use saturation potentials as high as 10,000 v. on the chamber, the possibility of corona from the guard wires had to be tested. At 15,000 v. a spark-over occurred at some point within the chamber but below this voltage no effect of corona was detectable with the current-measuring system.

The entire electrode assembly is mounted on a welded steel track running the full length of the cylinder. The displacement along the track is effected through a sprocket and gear drive operated from without the tank through a pressure-tight rotary Sylphon joint.

4. *Stray Ionization*

To avoid picking up any stray ions or electrostatic disturbances the entire conductor system leading from the collector plate to the electrometer was shielded. The collector itself is shielded by an aluminum cover (*D*). From there the conductor passes through two swivel joints (M_1 and M_2) and a section of telescoping tubing (*T*). From M_2 the lead passes down to a brushing contact on an insulated rod located centrally in tube *P* (1½ in.) extending the length of the track. A ½-in. sector of this tube is cut out at the top to permit insertion of the brushing contact. To close this long opening electrostatically, a strip of thin spring steel (*N*, Fig. 8) is stretched along the top and bottom passing over the rollers (*H*) at the ends, and moves with the chamber so as to always keep the slot covered. A gooseneck connection (*Q*) leads from the bushing (*S*) through a pressure-tight seal to the outside of the chamber. The entire electrical system is insulated with highly polished amber and no leakage difficulties have been experienced.

Careful tests were made to detect any stray ionization in this conductor system. The currents being normally measured by a null method, there should be no potential difference between the electrometer leads and the earthed shields. At normal working current sensitivites (10^{-13} to 10^{-14} amp. mm. deflection) no evidence of stray ionization currents was found even with an 8-in. entrant beam of x-rays. When a deflection method of measurement is used, the conductor may be at a potential several milli-

volts different from ground, but even under these conditions no stray ionization has been detected.

However, at the highest sensitivities (5×10^{-15} amp./mm.) various difficulties were encountered. Ionization from cosmic rays and alpha-particle contamination produced a slightly unsteady background current amounting to 3 or 4 per cent of the total measured current at atmospheric pressure. This was, of course, unavoidable.

Of greater concern was the effect of contact potentials within the insulated system at the very high sensitivities. These gave rise to very uncertain and unsteady stray ionization currents which varied with the plate separation, size of the x-ray beam, etc. These spurious effects were eventually reduced to a workable minimum even at our highest sensitivity. The greatest single source of stray ionization was between the guards and collector electrode where the spacing is only about 0.5 mm. This was largely eliminated by making the three plates out of a single sheet of aluminum, taking care that they were kept in the same relative position as before cutting. In addition, the inside of the tank was scraped and then painted with "Graphite Acid Seal" paint, which we had found by separate tests to establish little contact emf. with respect to aluminum or itself.

When using a broad beam at voltages above 360 kv., some radiation entered the front of the chamber through the several inches of steel making up the various flanges and supports. This was avoided by placing a lead baffle 3 ft. square and $\frac{1}{2}$ in. thick, on a frame in front of the chamber, with a 3-in. opening to permit passage of the x-ray beam. The $2\frac{1}{2}$-in. window at the fore end of the chamber was sealed with 0.5-mm. aluminum, which will withstand pressures up to at least 4 atm. In front of this is an electrically operated shutter and a rack for holding a large number of lead and copper filters, which could be shifted in and out of the x-ray beam from within the control room.

The entire assembled chamber was supported on a rigid frame, which, in turn, was mounted on a 20-ft. track running parallel to the useful x-ray beam. Thus target-diaphragm distances ranging from 2 to 6 m. were obtainable.

5. *Diaphragms*

Since the cross-sectional area of the limiting diaphragm appreciably affects the accuracy of measurement, it is essential that it be known with an accuracy of ±0.1 per cent. As pointed out in connection with previous high-voltage x-ray measurements, this is difficult of attainment and was finally reached through the use of hard-gold diaphragms made by pluggage methods [31, 32]. More recently it has been found possible to make hard-lead diaphragms by similar methods; relying for their final accuracy upon comparisons with the gold diaphragms. International agreement [33] requires that limiting diaphragms be cylindrical and of such thickness that not more than 0.1 per cent of the intensity of the useful transmitted beam passes through the walls of the diaphragm. The use of thick diaphragms necessitates great care in alignment in the beam since poor alignment reduces the effective area of the opening. Furthermore, at short diaphragm-target distances, a thick diaphragm introduces some uncertainty as to the proper position for placing a thimble chamber under calibration, or as to the application of any inverse-square law corrections.

There has been a tendency to use what we believe to be excessively thick diaphragms in the supervoltage x-ray region; for example, Mayneord [16] used a 3 cm. thickness at 400 kv. We, therefore, made some measurements to determine the minimum lead thickness to stop off 99.9 per cent of the incident radiation. Accordingly, the diaphragms, constructed as shown in Figure 11, were made of a thickness $2D$, where D is the thickness necessary to reduce the radiation to 1 per cent of its incident value, and $2D$ a thickness which will reduce the intensity to substantially less than 0.1 per cent. From *a* to *b* the ori-

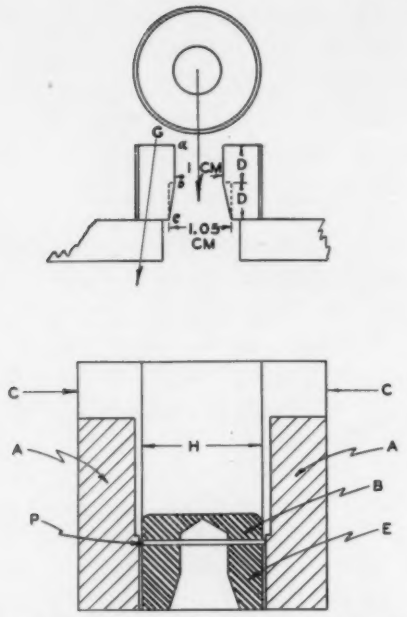

FIG. 11. Details of diaphragm construction.

fice is accurately cylindrical and from *b* to *c* it is tapered back to such a degree that the cross-sectional area at *c* is 10 per cent greater than at *a* and *b*. Thus even had the lead been cut away, as indicated by the dotted lines, the diaphragm would not have permitted the passage, through its body, of more than 0.1 per cent of the radiation passing through the orifice (assuming complete stoppage through *G*).

Values of *D* at different voltages were experimentally determined as shown in Table 1:

TABLE 1

REQUIRED DIAPHRAGM THICKNESSES FOR DIFFERENT EXCITATION VOLTAGES

Tube-voltage	*D* (1%)	*D*(0.1%)
kv.	mm.	mm.
240	3.4	6.0
300	5.5	9.2
360	6.7	12.0
400	8.2	16.0

Experience has also shown that to avoid distortion considerable care is required in the mechanical construction of the lead diaphragms. It has been found that a diaphragm held in a three-jaw chuck for the lathe operations will almost invariably distort after releasing, and use of a draw chuck does not usually permit a sufficiently accurate alignment of the hole. To make a diaphragm (*E*) we start with a solid block of brass through which a rough hole (*H*) is bored. This is partially filled with a hard lead alloy (Sb, Cd, Pb), which is forced into place with a rather high *steady* pressure (not hammer strokes). The block is then chucked at *C* and the portions *A–A* turned off. The lead (*E*) is then turned down to within about one or two thousandths of an inch of its finished size and cut off at *P*. After being allowed to age for a few days, a standard steel ball is gently forced back and forth through the opening to give it size as well as to burnish its surface.

6. *Saturation Voltage*

For the saturation voltage it was hoped to use direct current from a valve rectified alternating-current source. However, after trying out all the more common forms of voltage stabilization it was found to be impractical with the present very small capacity current-measuring system. Slow variations were not troublesome but irregular transients were. Several stabilizing devices which worked at a given voltage were impractical under the variable voltage requirements of our work. Large banks of radio B batteries were finally used.

IV. CURRENT MEASUREMENTS

The current measuring system is shown in Figure 12.

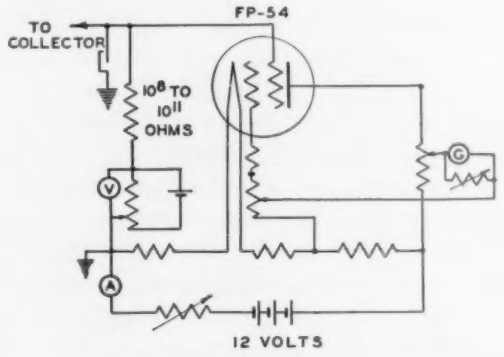

FIG. 12. Amplifier circuit.

The ionization current is amplified by means of an FP-54 electrometer tube in a balanced circuit of the type first described by Dubridge and Brown [34]. The modification of the original Dubridge-Brown circuit shown was suggested to us by Dr. Leo Behr in 1934; this, in common with all modifications since suggested, was designed to minimize the difficulty of balancing the amplifier network, but unfortunately, at the expense of some of the stability inherent in the original. With a galvanometer having a period of 3 sec. and a current sensitivity of 5.7×10^{-9} amp. mm. the voltage sensitivity of this system is 5.6×10^{-4} v./mm. With a grid resistor of 2.4×10^{-9} the current sensitivity is 2.3×10^{-13} amp./mm.; this sensitivity can be increased up to 50 times this value by increasing the grid resistance proportionately. The amplifier is linear to within 1 per cent for deflections up to the maximum obtained, as is shown in Figure 13.

Comparative current measurements are obtained by direct deflection; for absolute ionization-current measurements the system is used as a null measuring device. The voltage drop across the grid resistor is compensated by means of a potentiometer from the setting of which the voltage drop across the grid resistor is determined. If the resistance of the grid resistor is known, the ionization current can be determined. The grid resistors are of the S. S. White type used in this laboratory in a variety of circuits during the past 5 years. Tests of these resistors made in connection with

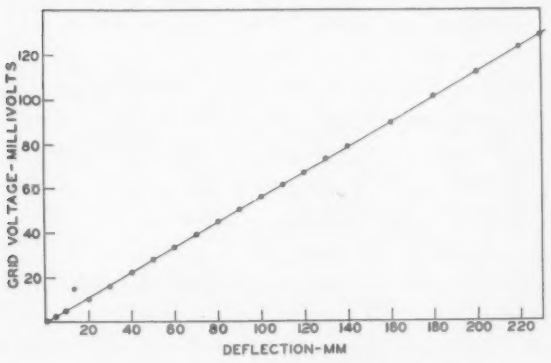

FIG. 13. Amplifier calibration curve.

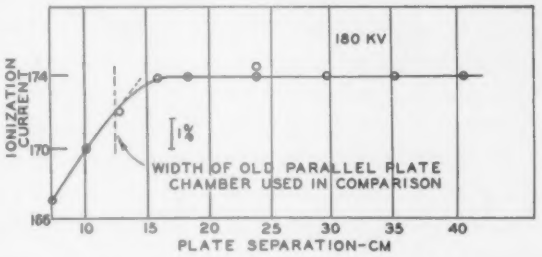

FIG. 14. Curve showing effect of plate spacing on field distortion for 180-kv. X-rays.

studies of x-ray ionization in liquids [35] has shown them to maintain their resistance values over long periods of time and have inspired confidence in their use. For absolute measurements, the grid resistor is calibrated by an electrostatic current compensator previously described [36], which is now used in the standardization of dosage meters.

The grid current of this amplifier is very small, being less than 10^{-4} times the ionization current measured; it is therefore possible to use this system as a null indicator in connection with an electrostatic compensator by simply removing the grid resistor.

The electrometer tube is shielded electrostatically and against radiation in a lead-covered cylindrical housing which is attached directly to the pressure ionization chamber. The tube proper is connected by means of a seven-wire shielded cable to the amplifier control panel, batteries, and galvanometer, all of which are placed inside the control room. The amplifier is remotely controlled by the observer from his station in the control room.

V. IONIZATION-CHAMBER CHARACTERISTICS

1. Field Distortion

In the 200-kv. guarded-field ionization chambers it was found that even with guard wires there was a minimum permissible distance between wires and the chamber ends beyond which error would be introduced [30, 31]. It was desired to check this in the new chamber as well as to be certain that the field correction was adequate at all plate spacings.

Accordingly, the electrodes were placed as near as possible (10 cm.) to the front of the chamber, set for a minimum separation and the guard wirds disconnected from the system. Using an 8-mm. beam of 180-kv. x-rays the ionization current was measured for several plate spacings up to about 15 cm. Repeating this with the guard wires connected, no detectable difference was found. Measurements of the ionization as a function of plate spacings (guard wires connected) are shown in Figure 14. Definite saturation is reached at 15 cm., which spacing happens to be about the limit beyond which field distortion should normally be encountered for a 25-cm. guard plate width, unless corrected with guard wires. That the curve is flat for spacings greater than 15 cm. proves the efficacy of the guard-wire system.

Comparisons were made between this pressure standard and an early type of free-air standard designed for 180 kv. [29]. (Mechanical difficulties prevented the use of our 200-kv. guarded-field standard, which, however, agrees with the one used within 0.2 per cent.) The same diaphragm and electrometer systems were used for both chambers so that the only factor entering the comparison was the effective plate length. Any further difference would have been due to such sources as spurious scattered radiation, stray ionization, etc. For a plate separation of 12 cm. in the low-voltage standard, and 24 cm. in the pressure standard, the latter indicated about 1.3 per cent high. Referring to the curve in Figure 14, it is seen that the 12 cm. spacing in the old chamber is probably deficient by about 1 per cent (as indicated by the ionization current). After making this 1 per cent correction, the two chambers agree within the limits of experimental error.

2. *Scattering from Diaphragm and Pressure-Chamber Ends*

The distance from the aluminum window at the front diaphragm to the collector electrode (in its closest position) is 59 cm., and while an effect of scattering from the thin aluminum entrant window upon the measured ionization seems unlikely, it was important to test therefor. In this connection, it may be stated that the indications of the chamber at high voltages will be unambiguous only if a state of electronic equilibrium exists in the region of the "ionized volume." Mayneord's [3, 4] and Lauritsen's [5, 6] analyses of this problem are very clear and it is felt that their fundamental conditions for electronic equilibrium must be met.

To test for scattering from the entrant window, the collector was moved as close as possible to the fore end of the pressure chamber and measurements made with the aluminum window, first in the normal position (5 cm. from the diaphragm) and then about 30 cm. in front of the diaphragm. The indicated ionization was the same for both cases within limits of measurement. The same was true for similar tests made with a 0.5-mm. copper window.

Further tests for scattering from the windows and for electronic equilibrium were effected by making ionization measurements at different positions of the collector plates along the length of the pressure chamber. The plate separation here was great enough to rule out any effect due to the beam divergence. Figure 15 shows a number of such curves at various excitation voltages. The 400-kv. curve was made at a chamber pressure of 2 atm. It will be noted that all the graphs are linear within ± 0.5 per cent or better, which agrees with the limits of accuracy at the time the measurements were made.

Scattering from the entrant window and diaphragm would show up as a sharp rise in the curve for small values of the distance between window and collector electrode. Similarly, scattering from the back of the chamber would cause a flattening of the curve at large values of the distance. Both are clearly absent. The linearity of the curves shows further that electronic equilibrium existed under all conditions of measurement.

Furthermore, from the slope of the

curves may be directly obtained the air-absorption coefficients with which it is necessary to correct all measurements. It is to be expected that the curves of Figure 15, representing absorption of the x-ray beam by air, should be linear within the range studied, since the attenuation is only about 5 per cent or less, and hence the change in quality is negligible. Air-absorption coefficients for several radiation qualities are listed in Table 2. These may be compared with similar determinations made at lower voltages [37]. The application of air-absorption corrections becomes particularly important at elevated chamber pressures.

Table 2

AIR-ABSORPTION COEFFICIENTS

Tube-voltage	Filter	Absorption per 100 cm of air	$\mu(cm^{-1})$
kv	mm	%	
240	1.2 Cu	4.77	48.8×10^{-5}
300	1.2 Cu	3.88	40.2
360	1.2 Cu+12 Al	1.50	14.9
400	1.2 Cu+12 Al	1.17	11.9

3. *Plate Separations*

To insure full utilization of the corpuscular emission from the air mass opposite the collector electrode, it is necessary to determine the minimum plate separation which will not cause a reduction in the measured ionization current. A number of such curves at different voltages are given in Figure 16. It will be seen that the minimum spacing is very definite in all cases and increases rapidly with the x-ray excitation voltage. This is decidedly at variance with the investigations cited in the introduction [16, 17].

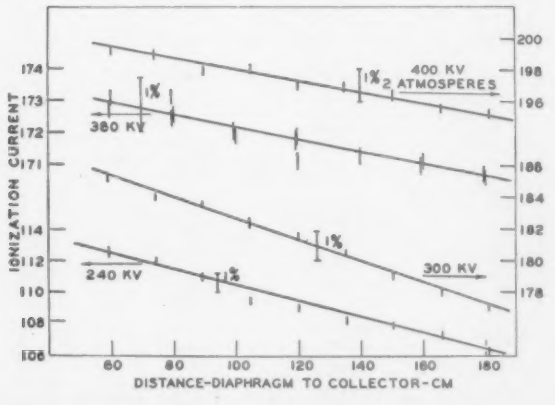

Fig. 15. Curves showing the ionization as a function of the distance between front diaphragm and collector electrode.

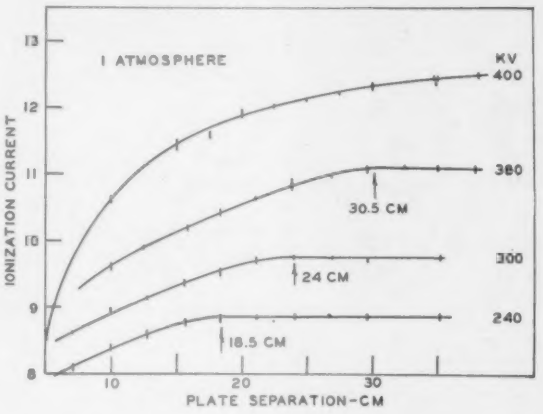

Fig. 16. Ionization as a function of plate separation for different X-ray voltages.

Particular attention is directed to the curves for 400-kv. radiation. The curve at atmospheric pressure cannot be said to definitely reach a steady maximum even at the greatest possible plate separation of about 40 cm. However, under a chamber pressure of 2 atm. the maximum is definitely reached at a plate separation of about 22 cm. This then fixes the working limits for the particular chamber. At atmospheric pressure, radiations up to 360 kv. can be measured; above 360 kv. elevated chamber pressures must be used. It is to be expected that a very considerable reduction in the size of the present chamber could be made by working at a pressure of 5 atm., but that has not been tested.

Failla [14], postulated the formation of an "electron cloud" to explain the limitation of his free-air ionization chamber in gamma-ray measurement. The possibility of a similar condition exists at 400 kv., where the scattering is predominantly in the forward direction and would show up as an apparent widening of the beam. This, in turn, would increase the necessary plate

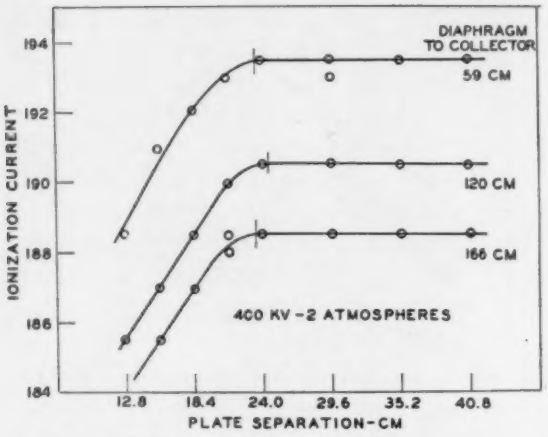

FIG. 17. Ionization as a function of plate separation for different diaphragm-collector distances.

separation for electronic equilibrium as the collector-diaphragm distance is increased. Figure 17 shows several plate-separation curves made at 400-kv. and 2-atm. chamber pressure, for the different collector-diaphragm distances shown. There is no evidence whatever of any cloud effect. Similar curves made at atmospheric pressure with 360-kv. x-rays likewise showed no cloud effect. This proves only that the cloud effect did not influence the measurements under present conditions. It may well be that it does exist here in principle, and that equilibrium obtained at our minimum distance of 59 cm. Such a condition, coupled with the fact that Mayneord and Jaeger used a much shorter diaphragm-collector distance than in our case, may contribute to the disagreement in the results.

4. Saturation

In all of the preceding work, sufficiently high potentials were used across the ionization chamber to insure full or nearly full current saturation. Tests showed that saturation is apparently not as easily obtained as indicated in some earlier work of others. It should be pointed out that "saturation" is not necessarily a definite thing and depends upon the degree of accuracy to which the measurements are made. According to Thomson's theory [42], which has been shown to represent the facts fairly closely, the degree of saturation required will depend upon the precision sought, and the maximum potential will vary as the square root of the precision. Moreover, the potential required for a definite saturation is proportional to the current for the simple case of uniform ionization. While this condition does not obtain in the case of a standard ionization chamber, the saturation voltage does increase with the density of the ionization.

It is not to be expected that radiation quality changes within the range here used should have any great effect upon the shape of the saturation curve. This is shown to be the case in Figure 18, which gives a group of saturation curves for excitation voltages ranging from 200 to 400 kv., but in which the intensities at saturation were all adjusted to the same value by moving the chamber away from the tube. It is clearly evident that within 0.5 per cent all curves are alike and reach saturation at the same voltage.

These curves may be compared with Mayneord's [16], which show saturation at 300 v. for a 20-cm. plate spacing, whereas our corresponding spacing was 32 cm. The conditions are not exactly comparable, but we do not find his change in form of the curve below saturation. Referring to Figure 18, it is seen that taking a value of 146 as representing saturation at 3,000 v., the chamber is within 10 per cent of satura-

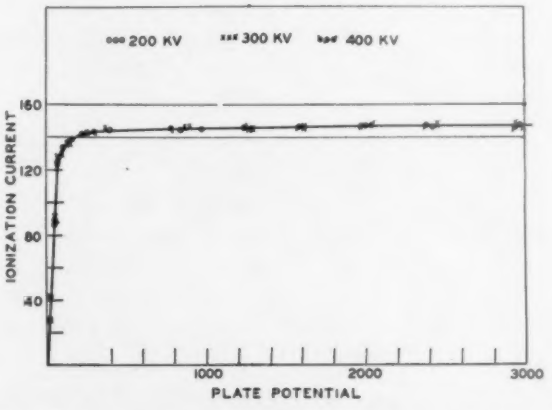

FIG. 18. Saturation curves for plate spacing of 30 cm. and different X-ray voltages.

tion at 90 v., 5 per cent at 160 v., and 1 per cent at about 1,000 v. Since our precision for the present measurements is about 0.5 per cent, there is no need to employ more than about 2,000 v. on the chamber. This lack of saturation at low voltages is also evident in Figure 19, which gives similar curves for smaller plate spacings.

A third set of saturation curves (Fig. 20) was made at a chamber pressure of 2 atm. Again, taking the current at 3,000 v. as saturated, the ionization chamber is within 10 per cent of saturation at 400 v., 5 per cent at 900 v., and 1 per cent at about 2,000 v. These results show the requirement of an approximate doubling of the saturation voltage at double the pressure, as might be expected.

5. *Ionization Measurements at Elevated Pressures*

Measurements already discussed have shown that the ionization chamber behaves normally, at slightly elevated pressures, with respect to plate separation, saturation, and electronic equilibrium. It remains, therefore, to insure that the ionization chamber actually measures all the ions produced at higher chamber pressures. Above 8 or 10 atm. Zanstra has shown that there is a definite loss of ions through volume or columnar recombination [40], so that the true ionization can only be inferred by applying the special methods devised by either Mohler and Taylor [41] or Zanstra [40].

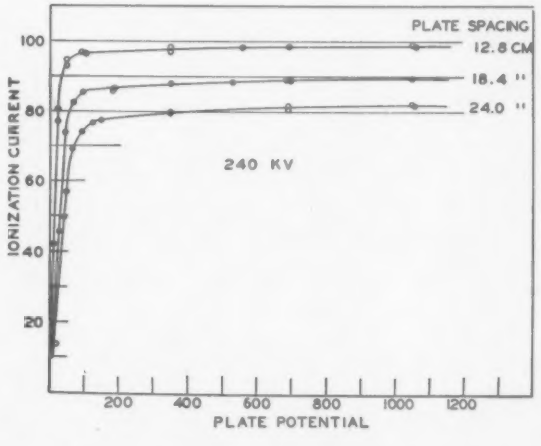

Fig. 19. Saturation curves at 240 kv. for different plate spacings.

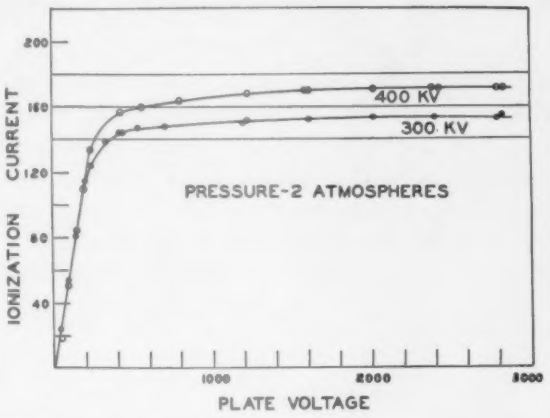

Fig. 20. Saturation curves at 2 atmospheres.

An accurate check of the possible loss has been made up to 3.3-atm. pressure. Figure 21 shows the ionization current as a function of the pressure in centimeters of mercury, the lower curve giving the current as actually measured. However, air absorption is relatively large and increases with pressure, so that this curve must be corrected for absorption between the diaphragm and collector, using the absorption data obtained from Table 2. The corrected curve is then seen to be a straight line within experimental errors. Accordingly, we may conclude that at least up to pressures of 3.3 atm. there is no appreciable loss of ionization because of recombination. This is in agreement with the recent work by Tanaka [38] at lower excitation voltages.

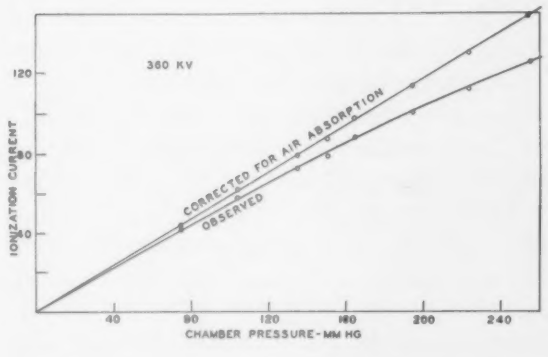

Fig. 21. Ionization current as a function of air pressure in chamber.

6. *Inverse-Square Law*

Application of the inverse-square law was tested for distances between target and chamber diaphragm ranging from 2.5 to 5.5 m. For this the chamber diaphragm was 1.5 cm. and the tube diaphragm 4 cm. in diameter. The results after correction for air absorption show close adherence to the inverse-square law, so that when necessary we may use it as a basis in calibration work.

VI. GENERAL CONCLUSIONS

From the measurements described above, we may conclude that it is feasible to construct a standard free-air ionization chamber for the measurement of supervoltage x-rays, although our basis for this conclusion rests upon physical factors, which differ decidedly from those of Jaeger [17], who reached the same conclusion. In particular, it is found to be possible to measure radiations of excitation potentials up to 360 kv. with a free-air chamber of moderate plate separation (30 cm.) at atmospheric pressure. For higher excitation voltages the ionization chamber may be kept within practical size limits by using it at slightly elevated pressures.

It appears, from these results, possible to construct an ionization chamber of very much smaller dimensions than herein used. Our own chamber was made its present size to permit the unhampered exploration of supervoltage measurements up to well over a million volts and possibly into the gamma-ray region. The results thus far indicate fair promise for extension to higher excitation voltages than used here.

Through the use of specially constructed x-ray generating equipment it is possible to make free-air ionization measurements in the supervoltage region with an accuracy comparable with that obtained in the high- and low-voltage region. There is thus provided a means for measuring the international roentgen by a means wholly independent of the thimble chamber and against which the thimble-chamber measurements may be compared. It is, therefore, possible to calibrate the clinical dosage meter under the same conditions as obtain for lower voltage radiations.

Some preliminary comparisons with thimble chambers yield reasonable results, but their description will be reserved until such later time as they may be carried out more fully.

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PROGRESS IN THE DESIGN OF ROTATING ANODE TUBES*

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CHICAGO, ILLINOIS

THE development of diagnostic roentgen-ray equipment has been largely motivated by a never-satisfied desire for greater roentgenographic speed and detail. Such is the motivation behind the idea of a rotating anode tube.

Although anode rotation was suggested early in the development of roentgen-ray tubes, and many mechanisms for its accomplishment have since been proposed, it is only recently that the technical means for practical realization have been available. One scheme was suggested as far back as 1897 (Fig. 1) by Wood.[1] In a tube of the earliest type, in which the glass bulb was still being used as a source of roentgen rays, he suggested rotating the complete tube except for the cathode, which was intended to remain in a fixed position in space due to gravity, and in this way give roentgen rays from a moving glass surface. There is no record that such a tube was built. Again in 1899, Rollins,[2] in several articles published in the *Electrical Review*, mentioned rotating targets. Although he referred primarily to movements between exposures, he also mentioned automatic rotation and apparently had in mind rotation during use of the tube.

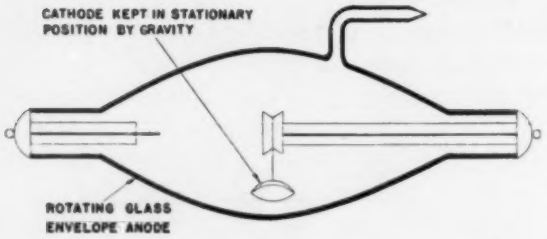

FIG. 1. Rotating tube with stationary cathode described by Wood, 1897.

There are no other significant references in the literature until 1914 when both Pohl[3] in Germany, and Thomson[4] in the United States, independently, and almost simultaneously, suggested new ideas in patent applications. Pohl, in addition to describing mechanisms for holding the cathode or anode stationary by gravity while rotating or vibrating the tube, also described schemes with magnets for rotating the anode only (Fig. 2). He apparently failed to appreciate the full possibilities of his suggestions because he limited them to therapy tubes, stating that they could not be applied to diagnostic tubes due to enlargement of the focal spot.

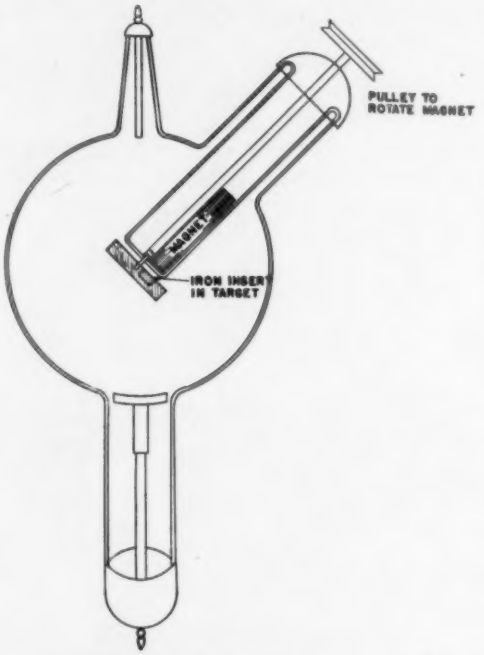

FIG. 2. Rotating anode tube shown by Ernst Pohl in German patent application, 1914.

Thomson, in his application, showed tubes of both the gas type and the newer high vacuum Coolidge type, having tungsten anodes in the shape of a wheel, mounted on dry graphite bearings, and rotated

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

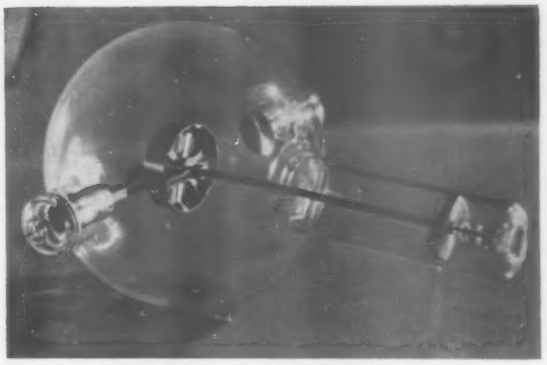

Fig. 3. Model of rotating anode tube by Elihu Thomson, 1914.

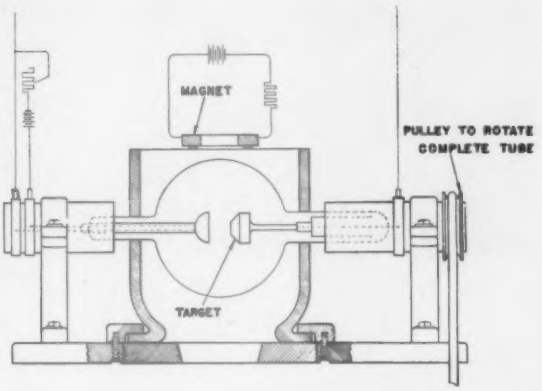

Fig. 5. Coolidge's rotating tube with magnetic deflection of the electron beam, 1915.

by magnetic means (Fig. 3). His work is important because he clearly conceived the problem and put his ideas in such practical form that engineering progress has followed closely along the lines of his formulation. Coolidge is somewhat responsible for this trend because he ran many experiments along the lines of Thomson's idea with encouraging results. Figure 4 shows a hot cathode, high vacuum rotating anode tube with ball bearings described in a report which he published in 1915.[5]

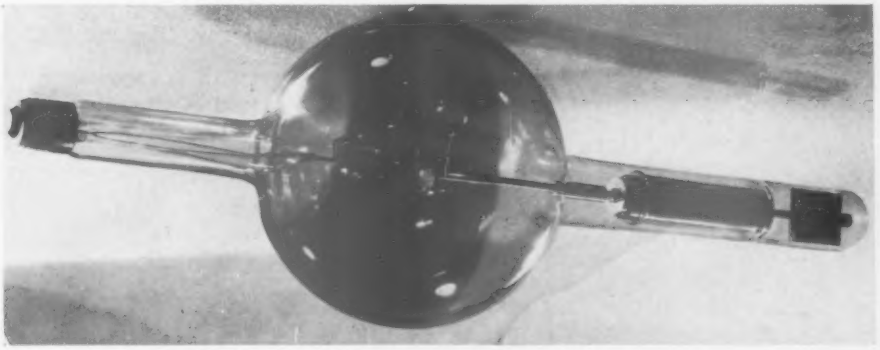

Fig. 4. Photograph of original high vacuum, hot cathode, rotating anode tube, built by W. D. Coolidge in 1915.

Coolidge also proposed and tried rotating the whole tube, using a magnetic field to deflect the electrons to a constant position in space[6] (Fig.5). This eliminated the problems of bearing rotation in a vacuum and of heat dissipation, but introduced a new problem of magnetic deflection of the electron beam. Although up to the present time the idea of rotating the anode only has seemed more practical than rotating the whole tube, it is conceivable that, in a field as new in engineering development as this, there might some day be renewed interest in the latter.

As an illustration of still another scheme, Muller, much later in England, built a tube in which continuous pumping allowed the anode to be brought to the outside and rotated through a vacuum stuffing box. He made tests and published data.[7] Although yet a laboratory device, this, too, with continued improvement in vacuum pumping equipment, may eventually have practical application. Other references in the literature, of which there are very few until recent years, deal primarily with engineering improvements on the older ideas. Some of the earliest include Schirmann[8] in 1920, Fujimoto[9] in 1922, and Bouwers[10] in 1927.

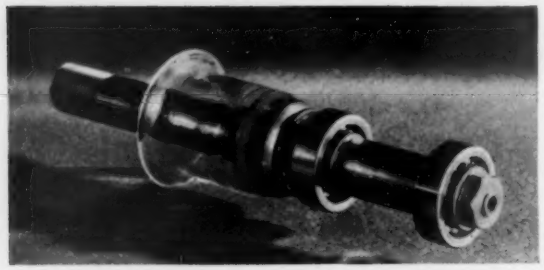

FIG. 6. Ball bearing assembly for rotating anode tube.

Progress in the practical realization of a rotating anode tube has been dependent upon advances in many fields, especially upon increased knowledge of the physical properties of materials, and upon advances in the field of roentgen tube design and manufacture. This is an excellent illustration of the dependence of progress in one field upon the advance of knowledge over the whole frontier of science. The problems involved in making a practical tube will be illustrated by describing one solution that has been reached in recent development work.

FUNDAMENTAL PROBLEMS

The fundamental problems of anode rotation in a vacuum are: (1) to obtain a bearing that will work without lubrication and without excessive deterioration; (2) to produce enough torque to overcome friction and insure rotation, and (3) to dissipate the heat generated in the production of roentgen rays. In many cases in the past the bearing problem has been needlessly complicated by lack of sufficient torque, in which case the need of low friction is added to the other bearing requirements. With our present experience, low friction seems difficult of attainment in a vacuum because molecules of adjacent surfaces are in more intimate contact than they would be in air, and there are no thin films of grease, oxide, or even oxygen to cushion the contact. In addition, the heat treatment, to which the bearing must be subjected during degassing of the tube, roughens its surface by causing explosions of gas from within the material.

Sliding surface bearing experiments were tried with various combinations of materials. Graphite, mentioned in Thomson's work of 1914, was tried in many combinations, as for example, graphite sliding on steel, copper impregnated with graphite sliding on different materials, and even sintered tungsten impregnated with graphite in different combinations. Other materials tried included quartz, silver, alloy steels of various combinations, tungsten-cobalt-chromium alloys, and sintered tungsten-copper combinations. All of these bearings deteriorated more rapidly than was considered satisfactory. Some of the same combinations, however, showed much more promising results when used in the form of ball or roller bearings. Eventually a ball bearing of special design and material was found that could be rotated 50 to 100 hours without any appreciable grinding or other deterioration (Fig. 6). This bearing will also stand temperatures as high as 650° C. for the short period of time during manufacture of the tube that is necessary in order to degass the anode structure.

In solving the torque problem, all possible advantage was taken of present day single-phase motor design. Surprisingly successful results were obtained by making a rotor in exactly the same form as that used in induction motors. It was found that special copper could be vacuum cast around oxide-coated silicon steel laminations without destroying the oxide coating, and that this structure could be thoroughly degassed (Fig. 7). This is attributable to modern vacuum and degassing technique and would not have been possible a few years ago. Design of an induction motor stator to transmit a rotating magnetic field across the necessary $\frac{3}{8}$ inch gap to the rotor, rather than across the few thousandths of an inch normally involved in a motor, was a relatively straightforward, although new, problem for motor designers. The end-result of all this is that with one-half horsepower input to the stator approximately one-twenty-fifth horsepower is made available to overcome friction in the tube.

Heat dissipation was found not to be as difficult a problem as it would have been a few years ago, because of progress in oil-immersed tube design. Of the three ways of transmitting heat—conduction, convection, and radiation—all are involved at different stages, in getting heat away from a rotating anode tube, but the actual transfer of heat from the anode structure to the outside of the tube involves radiation, primarily. Two alternative structures for heat radiation were tried: (1) a blackened surface copper anode of relatively large surface area, radiating both to the tube envelope and to the stationary parts of the anode structure, and (2) a tungsten disk anode having less surface area than the former, but capable of operation at higher temperature. Both proved practical; the tungsten disk structure was chosen in this particular case because of considerations other than of heat dissipation, namely, increased safety factor in case of accidental overload, reduced danger of failure from tungsten cracking, and longer focal spot path (Fig. 8).

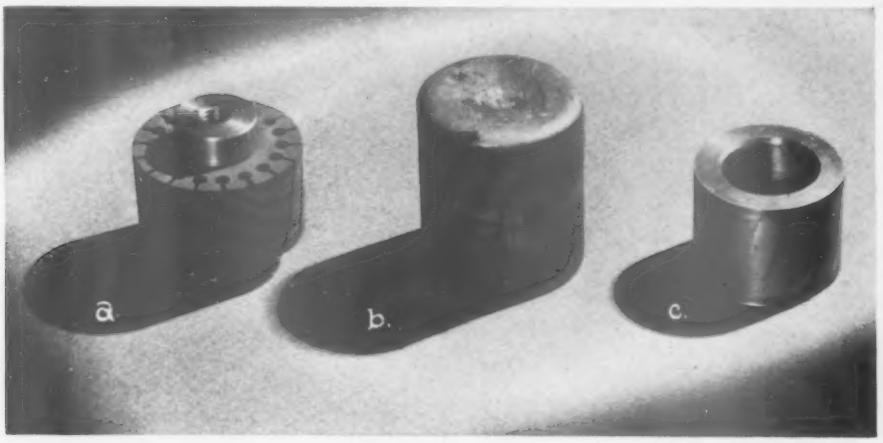

Fig. 7. Steps in the production of a vacuum cast rotor. *a*, iron laminations before casting in copper; *b*, completed vacuum casting; *c*, finished rotor.

Application to a Practical Tube

The engineering work involved in tube design is as important to a successful rotating anode tube as is the research necessary to solve the problems of rotation in a vacuum. Three objectives must be attained: (1) ruggedness and long life; (2) maximum rating and usefulness, and (3) minimum size and weight.

In these objectives oil immersion proved helpful. In addition to making possible the design and utilization of a small rugged tube, it provided a good cooling medium around the tube and a damping medium to prevent the building up of destructive vibration in the glass envelope. It also made practical the use of a bulb type envelope with consequently greater diameter tungsten disk than would otherwise be the case.

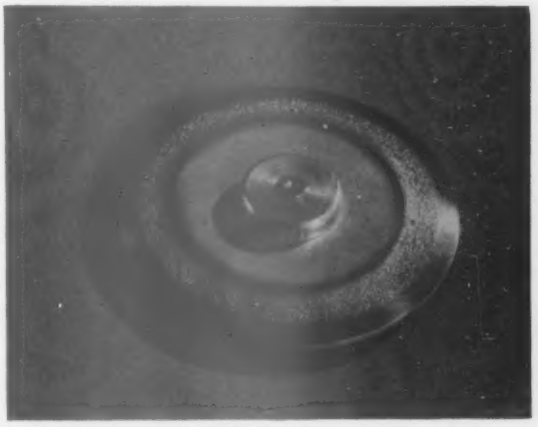

Fig. 8. Tungsten disk type of rotating anode after repeated overloads. (Although badly melted and showing many small cracks it still is in usable condition.)

Figure 9 shows certain details of the roentgen tube structure, and, in particular, of the anode. Note the large diameter tungsten disk joined through a molybdenum shaft of relatively poor heat conductivity to the rotor structure and bearings. Also note that the tube is held by a single support on its anode end, an arrangement that has been found to have definite advantages. Torque stresses between the induction motor stator and the anode rotor are transmitted directly through the stationary portion of the anode shaft without involving the glass envelope at all. No permanent stresses are put on the glass, as might be the case with two support points. Advantage is taken of a new metal alloy, called fernico, for the glass to metal seal,

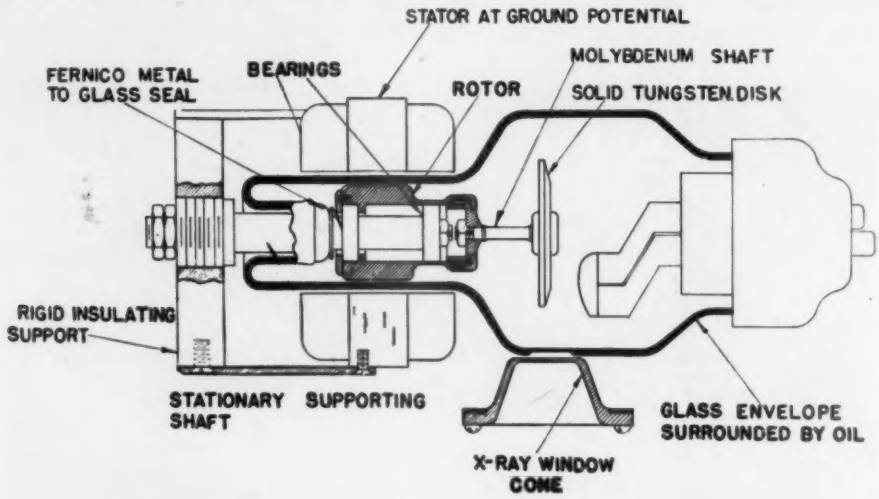

FIG. 9. Details of rotating anode tube and supporting structure.

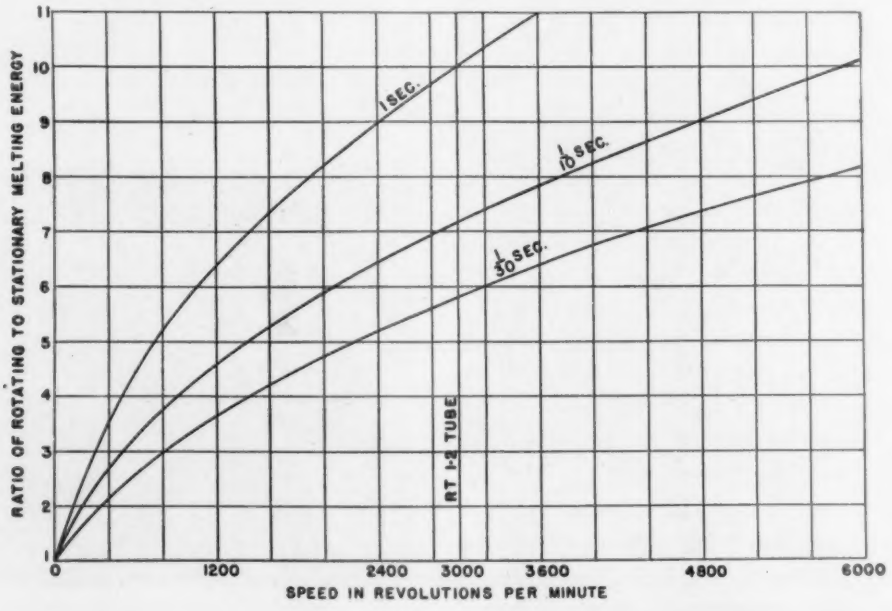

FIG. 10. Ratio of rotating to stationary melting energy as a function of the speed of rotation. 190 mm. focal spot path length; 15° anode; 1 or 2 mm. focal spot width. 60 cycle, single-phase, full-wave rectified circuit.

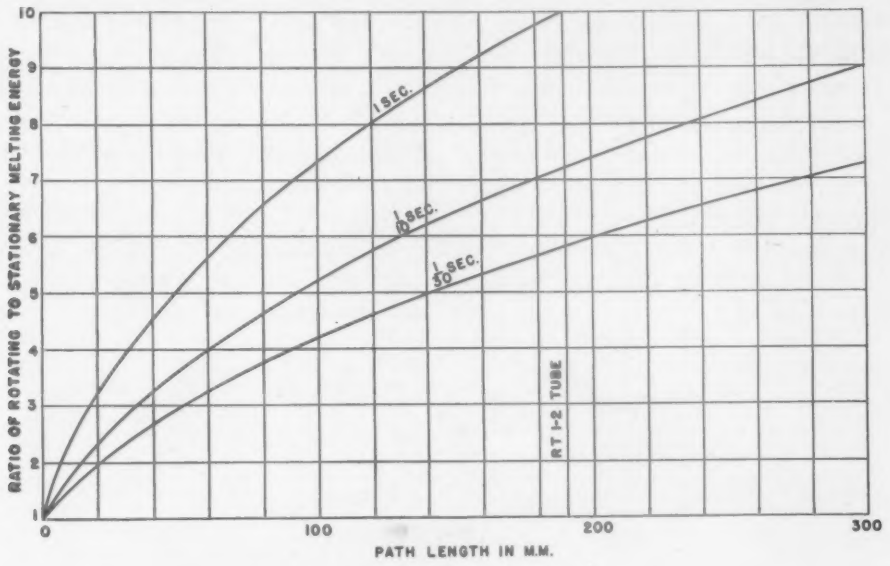

Fig. 11. Ratio of rotating to stationary melting energy as a function of the focal spot path length. 3,000 r.p.m.; 15° anode; 1 or 2 mm. focal spot width. 60 cycle, single-phase, full-wave rectified circuit.

which supports the weight of the glass envelope and of the cathode structure. This metal, developed primarily for the radio tube industry, makes a stronger joint than any of the other metals that have been available, as for example, copper, invar, or platinum.

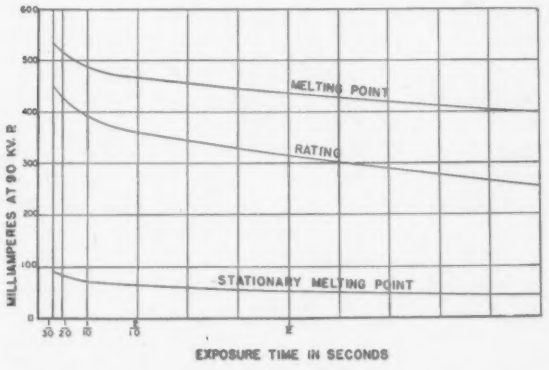

Fig. 12. Rating and melting energy as a function of time of exposure—2 mm. focal spot.

ENERGY CHARACTERISTICS

The energy characteristics of a rotating anode tube are difficult to describe clearly and simply because there are so many variable factors. This is especially true if attempts are made to compare with stationary target tubes of different focal spot size or shape. The only way of getting accurate comparative data is to determine experimentally the energies necessary to cause slight melting of the same focal spot in a single tube under the different conditions involved. In this paper, to avoid complication, all of the characteristic curves given are limited to single-phase full-wave rectified circuits, the type most widely used in the United States.

Figure 10 shows the influence of speed of rotation on energy capacity expressed as a ratio of rotating to stationary melt. For example, with a speed of rotation of 1,000 r.p.m., and a time of exposure of 1/10

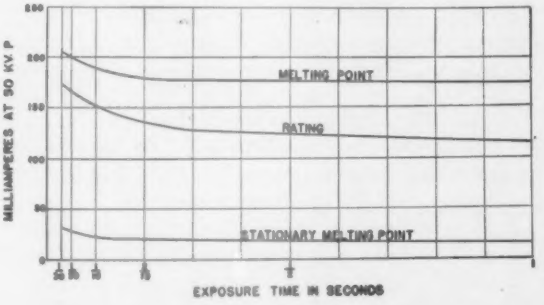

Fig. 13. Rating and melting energy as a function of time of exposure—1 mm. focal spot.

second, the energy capacity is 4.1 times as great as it would be if the anode were not rotating at all. If the speed of rotation is increased to 3,000 r.p.m. the energy capacity increases to 7.2 times the stationary capacity. The speed actually employed in any tube must be a compromise between desire for maximum gain and practical considerations of bearing design, ruggedness, and simplicity.

made possible by anode rotation. If so, and if a rotating anode tube is now a practical and reasonably economical tool—as it seems to be—it must surely play an increasingly important part in roentgenography. Continued and intensive development of rotating anode tubes is anticipated. As evidence of this, Figure 14 illustrates a very small rotating anode tube, still in the experimental stage, but which some day

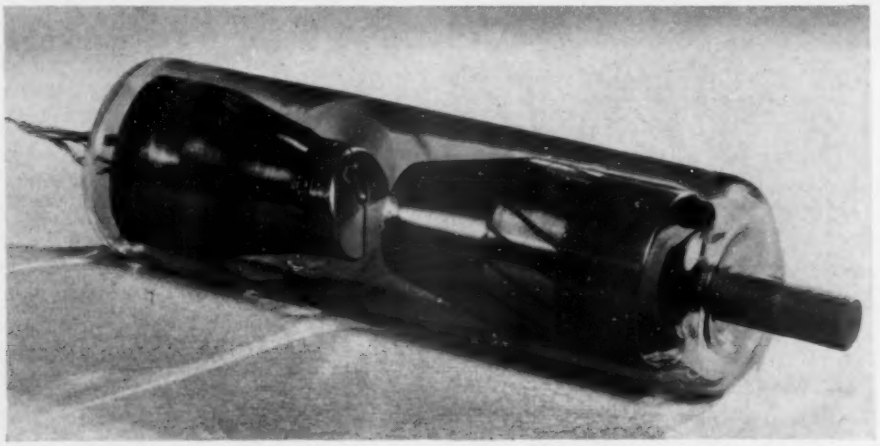

FIG. 14. Experimental small rotating anode tube.

Figure 11 shows the influence of focal spot path length on energy capacity, and illustrates the obvious conclusion that the path length, i.e., the anode diameter, should be as great as possible. In both these curves and in those shown in Figure 10 it may be observed that over most of the distance the energy capacity increases approximately as the square root of the focal spot path length or, in the case of Figure 10, of the speed of rotation.

Figure 12 shows the influence of time of exposure on energy capacity, and also indicates the relationship between melting point and rating energy adopted in this particular tube. Figure 13 gives the same relationships as Figure 12, but for a different size of focal spot.

CONCLUSION

The data presented in Figures 10 to 13 indicate that a radical improvement in roentgenographic speed and detail may be may be sufficiently practical to be incorporated into a small, but powerful, roentgen-ray unit.

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EDITORIAL

RADIATION THERAPY

SHOULD WE CONTINUE THE USE OF THE TERM "*SUPER*VOLTAGE"?

IT IS generally conceded that it is not a knife or a diathermy machine which cures an operable cancer: it is the skilful use of that knife or cutting current by a properly trained physician which results in a cure of that cancer. Should the surgeon use a longer or sharper knife than his colleague in another hospital, he is not apt to speak of his equipment as a "superknife." Despite great advances in recent years in the design and manufacture of Bard-Parker blades and electric "radio knives," most surgeons still speak of "surgical equipment" rather than "superequipment."

The practicing radiologist is confronted frequently by physicians or patients who want treatment with a "super" device. It may be a cancer of the skin; it may be an enlarged cervical lymph node. They still ask for, and believe they are missing something valuable if they do not get, *super*-voltage. This illogical state of affairs is attributable (*a*) to the human tendency to ascribe remarkable virtues to anything called new or super and (*b*) to careless use of the term supervoltage by those who are in a position to realize its limitations. That it is far from "super" in anything except psychological appeal is agreed by a number of observers.[1]

It would seem preferable that we use the simple term roentgen radiation, and speak as this as hard or medium in quality, or as possessing a certain half-value layer in copper. Thus, in the *average* installation, "supervoltage" would become hard roentgen rays (half-value layer 5 mm. Cu), and "200 kv." would be medium roentgen rays (half-value layer 1 mm. Cu), and so forth.

The following statements bear quotation in this connection, coming as they do from the pens of recognized authorities on this subject:

"Up to the present time there has been no scientific proof that the quality of radiation has an influence on the biological reaction. In the light of available evidence it would seem that the effects of radiation of different qualities are the same for equal amounts of absorbed energy."[2]

"If supervoltage is therapeutically useful, it is not because of better depth dose as we ordinarily measure depth dose. Tuve has calculated that one can improve the 10 cm. depth dose as much by going from 50 to 100 cm. target-skin distance as by going from 200 to 2000 kv (remaining at 50 cm.)."[3]

"Patients will inevitably assume that if 200 kv will almost cure cancer, surely 1,000,000 v will cure it easily. That is a proposition that will take a deal of proving! We will be wise to look carefully at the experience of the places now using supervoltage before we set up these costly installations everywhere. The advertising value of even 500,000 v, however, is bound to prove enormously tempting. Will patients and their physicians have the wisdom to inquire, not 'how many volts?' but 'what is the training and experience of the radiologist?' "[3]

"Thus the lethal action of radiation may be assumed to be independent of the wave length, a statement made nearly twenty years ago by Duane. . . . It is unlikely that the protein molecule of the cell is able to

[1] Stone, R. S. Skin reactions caused by 1,000 kilovolt and 200 kilovolt radiations. *Radiology*, 1938, *30*, 88–93.

[2] Pohle, E. A., Editor. Theoretical Principles of Roentgen Therapy. Lea & Febiger, Philadelphia, 1938, p. 158.

[3] Newell, R. R. Pp. 114–115 (see ref. 2).

recognize the source of the body which destroys it, any more than an individual shot through the head with a rifle can tell whether the bullet is of high velocity with a metallic sheath or an old-fashioned soft lead .45 caliber . . . "[4]

An additional reason for reconsideration of the term "supervoltage" is gained from a study of the actual results obtained in practice. In theory (and to the average physician), increasing the voltage should increase the depth dose to a considerable degree; in practice, owing to a more than neutralizing decrease in back-scatter (and for other reasons) it fails to do so.

Take the standard example of a mid-pelvic tumor. Let us assume that the patient has a *mid-pelvic tumor* and is of average dimensions, that is, *20 cm. thick* and *33 cm. wide*, and is to be treated at a 70 cm. target-skin distance. What is the actual tumor dose delivered by roentgen therapy techniques now in common usage, one employing ordinary voltage and one so-called supervoltage? The middle of the tumor is regarded as being 10 cm. from the skin of the anterior or posterior abdominal wall, and 16 cm. from the skin of the buttocks, when 60° oblique posterior portals are used. In the case of the latter it is to be noted that the scatter is much diminished by the non-scattering "air triangle" posteriorly. The figures given are from Quimby,[5] Glasser,[6] Packard[7] and Abersold.[8] By ordinary voltage is meant 200 kv. with half-value layer of 1.0 mm. Cu and by supervoltage 400 kv. with a half-value layer of 5.0 mm. Cu.

Under these conditions, with a patient of average dimensions, a mid-pelvic tumor given 2,400 r/air to each of two opposing fields, 15 cm. in diameter, receives by "ordinary" voltage radiation a dose of *2,496 r* at mid-tumor, while by "super" voltage it receives *2,544 r*, a gain of less than 2 per cent. Should we use a three-field technique, each field 15 cm. in diameter (one anterior, two posterior-oblique fields at 60°), 2,400 r/air to each, ordinary voltage delivers *2,522 r* at mid-tumor, "super" voltage *2,553 r*, a gain of less than 1 per cent.

We realize that some radiologists are beginning to believe that one can safely give much larger doses of hard than of medium quality roentgen rays, and that therefore in spite of diminished back-scatter, a significantly higher tumor dose can be delivered. Time alone will confirm the validity of these claims. In the interim, let us speak of high voltage roentgen rays in terms of quality as hard, medium or soft, and by stating the half-value layer of the beam in copper, and let us abandon the vague prefix "super."

L. H. Garland

[4] Wood, F. C. P. 203 (see ref. 2).
[5] Quimby, E. H. Personal communication.
[6] Glasser, O. Dosage measurement on ten 400 kv. roentgen-ray generators. Am. J. Roentgenol. & Rad. Therapy, 1937, *38*, 769–775.
[7] Packard, C. Calculation of percentage depth doses. *Radiology*, 1938, *30*, 613–621.
[8] Abersold, P. Personal communication.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Chicago, Ill., Sept. 19–22, 1939.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting, 1939: To be announced.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: St. Louis, Mo., May 15–19, 1939.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N.Y. Annual meeting, 1939: To be announced.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Special meetings may be called by the Chairman.

RADIOLOGICAL SECTION, LOS ANGELES CO. MED. SOC.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. Harry Hauser, 3395 Scranton Rd. Meetings are held at 6:30 P.M. at the Mid-Day Club rooms on the fourth Monday of each month from October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. E. A. Schmidt, 4200 E. 9th Ave., Denver, Colo. Meets third Tuesday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. J. H. Lucinian, 403 Huntington Bldg., Miami, Florida. Meetings held twice a year, May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets twice annually: in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. E. P. Halley, Decatur and Macon County Hospital, Decatur, Ill. Meetings held quarterly, time and place designated by president.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N.Y. Meets at Kings County Med. Soc. Bldg. on fourth Thursday, each month, October to May, 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. W. J. Marquis, 198 Clinton Ave, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Annual meeting, May, 1939. Exact time and place to be decided.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St., Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Fran-

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

cisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. H. C. Harrell, 517 Pine St., Texarkana, Texas. Next regular meeting in Temple, Texas, 1939.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgensellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

POINTS OF INTEREST

It is the purpose of the Inter-Society Committee for Radiology to promote the benefits to be derived from organized activity. Among other things the Committee encourages the formation of local, regional, and state societies of radiologists. Not only should these carry on the usual scientific programs, but they should take active and constant interest in the economic and social problems of radiology in their locality. Unethical practices by hospitals and their own members are questions deserving the attention of these local groups. The prevention of illegal practice by laymen, below-standard practice in eleemosynary institutions, exploitation and competition by hospitals and other corporations, the ethical promotion of early diagnosis and preventive medicine—all these are proper subjects for local action. Wherever possible, organized effort on the part of radiological groups should be carried on under the aegis and through the machinery of the county and state medical societies.

Among the news items in this month's Bulletin, the Inter-Society Committee calls attention to a few of the interesting developments and desirable projects by local and state radiological societies in various sections of the country.

* * *

Alert members of the *Pacific Roentgen Club* continue a winning battle to protect radiology against domination by corporate agencies and third parties in new economic experiments for medical care. The Medical Service Plan adopted by the California Medical Association on December 18, 1938, provides for pre-payment under an insurance plan to be supervised by the medical profession. Complete medical and hospital care is provided. Radiological bills are paid along with other medical bills and hospital care is defined as consisting of those non-medical services which a hospital is legally qualified to give, viz., bed, nursing, drugs, physiotherapy, and material appliances.

Efforts are being made to correct the recently inaugurated San Francisco Municipal Employees Health Service System which now includes an allowance for diagnostic medical procedures in its per diem payment to hospitals for hospitalized illnesses. Vigilance has not been relaxed in regard to the several hospital care insurance plans which, due to the efforts of the Club's officers, have agreed to confine their benefits to hospital services alone.

New rates for malpractice insurance imposed by the Insurance Commissioner of California will more than double the premium now paid by California members of the Radiological Society of North America and the American Roentgen Ray Society under their blanket agreement with Lloyds of London. These members are still endeavoring to secure an agreement that will permit them to retain their preferred rating.

The twenty-fourth issue of the *Bulletin of the Pacific Roentgen Club*, now a semi-annual publication, was issued last month.

* * *

Reports reaching the Inter-Society Committee are that the *Medical Society of West Virginia* has approved the adoption of hospital insurance plans, with the provision that benefits are to be defined by local county medical societies. It is presumed that county societies will follow the principle enunciated by the American Medical Association, requiring that no medical services be included as part of hospital care.

* * *

The secretary of the *Michigan State Medical Society* recently spent several days in the Inter-Society Committee offices for the purpose of discussing a proposed hospital insurance plan to be directed by the state society. Hospitals in Detroit have created a plan of their own. Radiology is not included as a hospital benefit.

* * *

Nearly every state medical association in the country is investigating the desirability of perfecting a non-profit insurance plan for the prepayment of medical bills for low income patients. *North Carolina* is not excluded. Radiologists there report that the proposed plan will reimburse policy holders for services received from radiological specialists in the same manner that other medical and surgical benefits are provided.

An interesting fiscal arrangement for hospital practice has been accepted by radiologists working in one Asheville hospital. In the case of charity patients, the physicians contribute their services and the hospital contributes supplies and the use of its equipment. Pay patients receive a bill for all radiological charges on the physician's billhead. Collections are held in trust by the hospital cashier. All receipts are turned over to the radiologists, who reimburse the hospital for expenses incurred in maintaining the department on an arbitrary basis of two dollars for each film used on a private patient.

* * *

The Council of the *Illinois Medical Society* has adopted a resolution that was distributed by the Inter-Society Committee last year to its list of state representatives. The resolution clarifies certain principles pertaining to the relationships between physicians and hospitals. Among other things it demands that, "No hospital shall offer, for a price, any medical service." The same resolution has been adopted by the Wyandotte County Medical Society (Kansas), the Hillsborough County Medical Society (Florida). It has been approved in modified form by several other county and state societies. Interested members may receive copies of the complete resolution by writing to the Inter-Society Committee office.

* * *

The *Nebraska Radiological Society* prepared a resolution, which was introduced at the last annual meeting of the state society, calling upon the society to affirm the action of the American Medical Association in regard to relations between hospitals and radiologists. It resolved that all services connected with the practice of radiology should be under the direct control and supervision of the medical profession. At the request of the Radiological Society, the Omaha-Douglas county society has forbidden the inclusion of radiology as part of hospital care in a proposed hospital insurance plan.

* * *

In addition to its annual scientific conference in the summer, the *Denver Radiological Club* maintains an active interest in the economic problems of radiology. Members were successful last year in defeating attempts by local hospitals to include radiological services as a part of their care in a hospital insurance plan. The Colorado State Medical Society was brilliantly successful in defeating a bold attempt by chiropractors to amend the state constitution in such a manner as to permit them to engage in medical diagnosis and treatment. The amendment was overwhelmingly defeated in the last state election.

* * *

Radiological practice will benefit from two decisions recently made by organized medicine in *Oregon*. A special committee has been appointed by the state society to make an investigation and recommendations relative to the status of radiologists and pathologists in hospitals in connection with a medical insurance plan to be operated by the medical profession. The Multnomah County Medical Society (Portland) has requested that a charge of three dollars be made to insurance companies for all reports pertaining to applicants or claimants. This action will eliminate attempts by insurance carriers to secure certified statements by radiologists without paying a fee.

* * *

The following resolution and motion were unanimously adopted at the San An-

tonio meeting of the *Texas Radiological Society* on October 22, 1938:

WHEREAS, The science and art of radiology is a recognized specialty in the practice of medicine, and

WHEREAS, The hospitals supported by the State of Texas, the Veterans Bureau and the Public Health Service are justly models for other hospitals, both private and charitable, and

WHEREAS, One of the requirements for Class A hospital rating recommends that the department of radiology be headed by a radiologist,

Be It Resolved, That the Texas Radiological Society, meeting in regular session, recommends that each of the hospitals supported by the State of Texas, the Veterans Bureau and the United States Public Health Service have a properly qualified radiologist, preferably a diplomate of the American Board of Radiology, head their individual radiological departments.

The resolution was indorsed by the Texas State Board of Health at its annual meeting in December. The Texas State Medical Association will be asked to adopt it at the next annual session.

* * *

A schedule of fees for industrial work adopted by the *Iowa X-Ray Club* a number of years ago has been enthusiastically supported by industrial insurance companies. It has eliminated the evil of occasional fees below the actual cost of complete and careful examination. Both radiologists and insurance companies are well pleased with the results of the project.

Iowa radiologists have likewise adopted a method for charging fees to the U. S. Employees Compensation Commission which assures a fair and adequate fee for examination of traumatic injuries suffered by workers employed by the Federal Government. The fee schedule issued by the Employees Compensation Commission was proposed by the American Hospital Association and defrays the cost of technical work only. The inequities of the schedule have caused consternation and complaint by radiologists throughout the country. In Iowa, radiologists add a fair and reasonable fee for consultation to the ECC fee for technical work bringing the total to equal the charge allowed by the industrial fee schedule mentioned above. These fees are paid by the ECC without objection.

* * *

Dismissal of the radiological staff of the Tampa Municipal Hospital and discharge of the hospital superintendent, followed by appointment of one man to serve in the dual capacity of superintendent-radiologist, started a controversy in *Florida* which culminated in a wholesale war involving the county medical society, the hospital trustees, and the mayor, and attracted the attention of the American Hospital Association, the American College of Surgeons, and the American Medical Association. After months of debate, a new superintendent was appointed on December 13, 1938. The salaried radiologist remains, however, supplanting the former staff which reimbursed the hospital on a percentage basis for its expenses in maintaining the department.

Following initial objections by the hospital staff and the county medical society, the hospital trustees received a letter from Bert W. Caldwell, secretary of the American Hospital Association, congratulating the board upon its action and applauding the employment of a salaried radiologist as "good business as well as good administrative policy." Thereupon the American College of Surgeons removed the hospital from its approved list on the grounds that the dual responsibilities of superintendent and radiologist could not be successfully combined in the hospital. Before the board of trustees had complied with the demands of the College of Surgeons, they received another request from the American Medical Association's Council on Medical Education and Hospitals to take additional steps to comply with the principles of the Council. Besides replacing the superintendent, the board discharged from the staff fourteen doctors who were not members of the county medical society.

The following resolution, introduced by Dr. Stanley A. Clark, president of the *Indiana Roentgen Ray Society*, and Dr. A. S. Giordano, president of the Indiana Association of Pathologists, was adopted by the Indiana State Medical Association at its annual meeting on October 4, 1938:

Whereas, The American Medical Association has through its House of Delegates and its various bureaus and councils from time to time propounded certain principles of ethics and established standards of relationships looking toward the maintenance of the highest quality of professional service both in private practice and in hospitals; and

Whereas, Many of these pronouncements refer specifically to those special branches of medicine involving somewhat unusual relationship between hospital institutions and the physician practicing these specialties in the hospital; and

Whereas, Certain usages have sprung up which are tending to involve ethical and legal consideration; and

Whereas, It would appear to be highly desirable and in the best interests of good medical practice and sound public policy to have certain of the aforementioned pronouncements clarified, codified and in some instances reiterated; and

Whereas, At the last meeting of the American Medical Association at San Francisco in June, 1938, a resolution requesting the Council on Medical Education and Hospitals to study the status of clinical and pathologic laboratories, and radiologic departments in hospitals and institutions with a view toward standardizing the relationship of these services to these institutions and when necessary reaffirming principles of ethics involved in these relationships; and

Whereas, The practice of medicine combines the exercise of professional knowledge and judgment and technical skill; and

Whereas, Hospitals and other lay organizations associated with physicians in the care of the sick find it essential to have available competent departments of roentgenology and clinical pathology; and

Whereas, Physicians especially trained in the selection, use and interpretation of diagnostic aids in clinical pathology and roentgenology are a recognized necessity in medical practice; and

Whereas, The technical skill required in the practice of roentgenology and clinical pathology needs to be supplemented by the professional knowledge and judgment of a physician before it is used in the diagnosis and treatment of disease; therefore:

Be It Resolved, That the Indiana State Medical Association reaffirm the action of the House of Delegates of the American Medical Association, 'that the practice of clinical pathology and roentgenology is the practice of medicine,' and recommends that clinical and roentgenological laboratory services be excluded from service contracts which exclude other professional services; and

Whereas, Our duty to the sick and afflicted is to furnish the best service possible; therefore

Be It Further Resolved, That all laboratories practicing these specialties should be recognized as being ethical only when they are operated and supervised by a physician trained and recognized as being competent in these specialties in medicine, and

Be It Further Resolved, That laboratories, which indulge in unfair competition by wholesale advertising of cut-rate prices, be specifically classed as unethical and unworthy of support by ethical members of the profession.

Mac F. Cahal
Executive Secretary

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

The first American Congress devoted to a consideration of medical, nursing and other problems associated with human reproduction will be held in the Municipal Auditorium, Cleveland, Ohio, from September 11 to 15, 1939, inclusive. It will be designated as The American Congress on Obstetrics and Gynecology. The promotion and sponsorship of the Congress has been delegated to the American Committee on Maternal Welfare, Inc. The latter includes the following organizations in its membership:

American Association of Obstetricians, Gynecologists and Abdominal Surgeons
American College of Surgeons
American Gynecological Society
American Hospital Association
American Nurses Association
American Protestant Hospital Association
American Medical Association Section on Obstetrics and Gynecology
American Public Health Association
Central Association of Obstetricians and Gynecologists
Chicago Maternity Center
Maternity Center Association of New York
National Medical Association
National League of Nursing
National Organization for Public Health Nursing
New England Obstetrical and Gynecological Society
Pacific Coast Society of Obstetrics and Gynecology
Southern Medical Association
U.S. Bureau of the Census
U.S. Children's Bureau
U.S. Public Health Service

The purpose of this Congress is to afford opportunities for discussing and publicizing the problems associated with human reproduction and the health of women and newborn babies. The value of more generally disseminated knowledge about the processes and problems of human reproduction and of the special diseases of the female generative organs and the newborn is important in the maintenance of public health and therefore the interest of woman's welfare extends not only to the medical profession but to associated groups, including nurses, public health officials, hospital administrators, eugenists and many others.

Problems develop with the expansion of knowledge and these can be discussed most effectively at a meeting where many viewpoints can be intelligently discussed. Congresses, international and national, afford the means of presenting and discussing the advances in various fields of science and bringing them to public attention. Obstetrics and gynecology in particular demand that wider association with allied groups, aside from the practitioners of medicine, which is so essential to the progress and welfare of the public. For these reasons the scope of the projected Congress has been extended beyond that of similar assemblies held in the past and will devote much attention to the wider public welfare aspects of problems which have been considered frequently of purely medical interest.

The last International Congress of Obstetrics and Gynecology was held in Amsterdam, Holland, in May, 1938. Its success stimulated a desire to hold a subsequent one in five years in another European country. It is felt that the difficulties associated with an international assembly, such as languages, expense, long distance travel, and limited participation, lack of common interest, call for a regional gathering in which opportunities for more general discussions would prevail. The proposed American Congress will therefore be modeled on different lines and will include participation not only by medical groups but by those devoted, as already stated, to nursing, public health and institutional administration. The program will provide morning, afternoon and evening sessions.

In addition to the scientific sessions it is planned to provide for several evening meetings at which speakers of prominence will discuss the broader aspects of the subjects for the lay public. There will also be prepared a comprehensive exhibit—scientific, educational, technical and commercial, which should add greatly to the general interest of the Congress.

National, sectional and local specialist societies have approved the Congress and have made contributions for its support. It is desired that a wider representation be secured through the medium of contributing memberships, the cost of which has been placed at five dollars. Application may be made at the office of the Congress, 650 Rush Street, Chicago, Illinois. Also any further information desired will be available at this office. Early application is desirable and will serve as an indication of personal interest in the success of the undertaking.

PRESENTATION OF A MEDAL TO DR. BELOT

On December 13, 1938, at the Marcellin-Berthelot Center in Paris, Dr. J. Belot was presented with a medal in honor of his contributions to Radiology as an investigator and a teacher. Dr. Belot is the Director of the Department of Radiology at the Saint-Louis and the Villejuif Hospitals in Paris. Leader of the French delegation, many Americans had the pleasure of meeting him at the Fifth International Congress of Radiology in Chicago in September, 1937. The medal was prepared at the instance of his many friends and students. The presentation took place before a large assembly which included radiologists from several foreign countries as well as his colleagues in France, professors of the faculty of medicine, and doctors from the various Paris hospitals. A number of laudatory speeches were made, outlining Dr. Belot's life and his career as a radiologist. His American friends wish to add their congratulations to those of his European colleagues upon this well deserved honor.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return or the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

MENINGIOMAS: Their Classification, Regional Behaviour, Life History, and Surgical End Results. By Harvey Cushing, M.D., Sometime Associate Professor of Surgery, Johns Hopkins University; Moseley Professor of Surgery, Harvard University, and Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston; Sterling Professor of Neurology, Yale University. With the collaboration of Louise Eisenhardt, M.D., Assistant Professor of Pathology, Yale University School of Medicine; formerly Associate in Surgery, Peter Bent Brigham Hospital, Boston. Cloth. Price, $15.00. Pp. 785, with 685 illustrations. Springfield, Illinois: Charles C. Thomas, 1938.

This is a masterpiece of the type that we have learned to expect from the facile pen of Harvey Cushing. Here he and Dr. Eisenhardt have considered the tumors arising from the meninges from every aspect. Aside from Chapter v, some twenty-five pages in length, devoted to the meningiomas and neurinomas of the spinal canal, of which the authors had experience with twenty-nine, the book is a discussion of the intracranial neoplasms. Their experience included 295 such cases. There is a thorough consideration of the pathology of these tumors in which all of the possible variations in the gross appearance and microscopic structure are discussed. Dr. Cushing was one of the first to point out the important fact that meningiomas have a predilection for certain definite sites. In this book the cases have been grouped according to the location of the tumor and the symptoms, findings, treatment and prognosis have been discussed on this basis. Thus there are chapters devoted to the suprasellar meningiomas, the olfactory groove meningiomas, the meningiomas of the sphenoidal ridge, etc., etc. There is also a chapter dealing with surgical technique and complications. The authors are to be highly complimented on the fact that all but two cases have been followed throughout the postoperative period. As a result of this study they are able to state that the average operative mortality for the intracranial meningiomas was 10.5 per cent, the case mortality (some patients were operated upon more than once) was 19.6 per cent. For the 120 patients seen in the last five year period (1927–1932), the operative mortality was 8.3 per cent and the case mortality 11.8 per cent. Of even greater interest is the fact that of the 226 patients who survived the operations 172, or 76 per cent, lived for five or more years thereafter, 81, or 36 per cent, for ten or more years, and 132 were still alive when the book was written.

Of the entire book Chapter XXXI, which relates the tragic stories of Timothy Donovan and Dorothy Russell, stands out as the literary peak. A more moving story of human endurance and perseverance has rarely been written. The story of the case of General Leonard Wood will also be of interest to many readers quite apart from its scientific value.

In only one respect is our enthusiasm for this book in the least dampened. Dr. Cushing has wholeheartedly supported the thesis of the traumatic origin of these tumors. This uncritical acceptance of the patients' rationalizations concerning the origin of their disabilities, which is of a similar type in many other cerebral disorders, such as psychoses, feeblemindedness, etc., would be of little consequence were it not for the fact that it will have many and serious reverberations within our courts.

The publisher is to be complimented upon the excellence of his work. The letterpress is good, there are amazingly few typographical errors, the illustrations are well reproduced. There is an extensive bibliography and a satisfactory index.

PAUL C. BUCY

THIRD SYMPOSIUM ON SILICOSIS: An Official Transcript of the Third Silicosis Symposium held in connection with the Trudeau School of Tuberculosis at Saranac Lake, N. Y., June 21 to 25, 1937. Paper. Price, $3.00. Pp. 266. Edited by B. E. Kuechle, Vice-President and Claims Manager, Employers Mutual Liability Insurance Co., Wausau, Wis., 1937.

In this monograph are authoritative articles by the outstanding men in the field of silicosis

and the subject is considered from all of its many-sided aspects. There are chapters on the etiology, pathology, physiology, roentgenology and one on the clinical picture of silicosis with a consideration of disability. The problem of measurement of dust concentrations and the control of silicosis both from medical aspects and as an engineering problem are adequately covered. The administrative aspects, legislative control and compensation are also included.

Some of the important parts of this monograph are given in brief below.

Silicosis is a widespread menace as 500,000 persons are exposed to silica dust of whom about 25 per cent will develop some clinical symptoms from silicosis. The commonest form of crystalline silica is quartz (silicon dioxide) and of amorphous or non-crystalline silica is opal ($SiO_2 \cdot H_2O$). The size of the particles determines whether or not the dust will be harmful. If the particles are more than 10μ in diameter they will settle out of the air rapidly and will not cause any damage. The very small particles around 0.5 to 5μ are the most dangerous as they are able to enter the smallest air passages. Large quantities of coarser inhaled dust particles are filtered out or caught on the mucous membranes of the upper air passages and are eliminated in the sputum without causing any damage. The individual anatomy of the finer air passages plays an important part in individual susceptibility. It is apparently not the shape of the particles or their hardness which causes the damage but a chemical reaction of silica which causes the local deleterious effect. A typical and acute reaction can be produced in various organs of animals by injecting the silica particles intravenously.

In the United States estimates of dust concentration are usually made by the impinger apparatus in which the dust from known volumes of air is trapped in water and the particles counted in much the same way as blood cells are counted. Although there are some practical objections to the method, it is in such widespread use that it has become the standard in this country. In England dustiness is measured by the thermal precipitator and in South Africa by the konimeter and sugar tube.

In studying the pathology of silicosis, large sections of the diseased lung are cut and petrographic examinations are made, using special technique to demonstrate the particles of silica. Histologically one finds cells engorged with particles of silica, many of the cells having been killed, others having formed giant cells. Some of the cells have carried the dust to the lymphatics where nodules are formed. These nodules reduce the flow of lymph in the lungs causing a local fibrosis and eventually decreasing the vascularity.

In contrast with the nonspecific dust reaction which causes no permanent damage and only a slight increase in the susceptibility to tuberculosis, the silicotic reaction causes a marked increase in the susceptibility to tuberculosis estimated at 60 per cent. The silicotic reaction is divided into two types: I, simple silicosis when there is no associated infection; II, silicosis complicated by tuberculosis, the so-called silicotuberculosis. There are two stages of the silicotic reaction in the normal lung. The first stage is one of benign perilymphatic reaction causing a diffuse thickening of the peribronchial markings in the roentgenogram. The second stage is more advanced and is one of discrete nodulation. The characteristic nodules are about 3 mm.in diameter, scattered throughout the lung fields, more marked in the mesial portion around the hila and in the bases. The periphery of the lung for a distance of about 2 cm. remains clear. This particular distribution is thought to be the result of a massaging action of the increased expansion and contraction of the periphery of the lungs. This forces the dust particles mesially in the lymphatics.

In silicotuberculosis one finds massive reactions of conglomerate fibrosis resulting from the accumulation of dust particles and blockage of the lymphatics. There is a synergistic reaction between silica and tuberculosis which produces this conglomerate reaction. As a result of the fibrosis, there is a marked reduction in the capillary bed of the lung, an increase in the residual air, a decrease in the tidal air and a decreased oxygen saturation. This will result clinically in dyspnea on exertion with right axis deviation and right ventricular hypertrophy in the electrocardiographic tracings but no cyanosis or clubbing of the fingers and only a slight polycythemia.

Roentgen examination permits differentiation of the two forms. The finding of the simple nodular form with no evidence of tuberculosis is compatible with good life expectancy and the diagnosis of simple silicosis. The presence of progressive conglomerate fibrosis with dis-

tortion of the lung anatomy, evidence of pleurisy, emphysema at the bases and cavity formation all superimposed on the primary complex is designated as silicotuberculosis. The conglomerate fibrosis usually results in a breakdown of the avascular fibrotic areas with cavity formation and eventually death from tuberculosis.

Roentgen examination is the most important and most valuable method of diagnosis, but the diagnosis should not be made without an adequate case history and a knowledge of the character and quantity of dust to which the patient has been exposed, and the duration of exposure.

There are also important chapters on the control of the quantity of dust, the engineering aspects of the problem, control by legislation, and the compensation aspects. On the whole, this monograph is an excellent summary of our present knowledge of silicosis and should be in the library of everyone who sees or expects to see cases of silicosis.

MERRILL C. SOSMAN

INTRODUCTION TO OPHTHALMOLOGY. By Peter C. Kronfeld, M.D., Professor of Ophthalmology, Peiping Union Medical College. Cloth. Price, $3.50. Pp. 331, with 32 illustrations. Springfield, Illinois: Charles C. Thomas, 1938.

The purpose of this textbook, according to the author, has been "to formulate the principles underlying that portion of Ophthalmology which is a necessary part of basic medical education." The intentions thus expressed have been carried out in a logical way. Numerous details as to methods of examination and treatment have been omitted. The book opens with an anatomical introduction and then considers diseases of the anterior portion of the eye, the cornea, uveitis, endophthalmitis, lens, and injuries. Physiology, retinal circulation and vascular diseases of the eye are next considered. There is some consideration given the neoplasms, disease of the optic nerve and the visual pathways. Consideration is also given to the pupil and an outline of the subject of refraction.

The book is beautifully designed, bound and printed. The plates used are in black and white. A novel feature is an ophthalmic dictionary. This is rather incomplete and combined with the index is somewhat confusing.

The book may be said to include material which should be given to the undergraduate medical student and is adequate to supplement most practical courses given in undergraduate medical schools.

PARKER HEATH

BOOKS RECEIVED

OUTLINE OF ROENTGEN DIAGNOSIS: An Orientation in the Basic Principles of Diagnosis by the Roentgen Method. By Leo G. Rigler, B.S., M.B., M.D., Professor of Radiology, University of Minnesota, Minneapolis, Minnesota. Atlas Edition. Cloth. Price, $6.50. Pp. 212, with 254 illustrations shown in 227 figures, presented in drawings and reproductions of roentgenograms. Philadelphia: J. B. Lippincott Company, 1938.

CLINICAL ROENTGENOLOGY OF THE DIGESTIVE TRACT. By Maurice Feldman, M.D., Assistant Professor of Gastroenterology, University of Maryland; Associate Roentgenologist, Sinai Hospital; Assistant in Gastroenterology, Mercy Hospital, Baltimore, Maryland. Cloth. Price, $10,00. Pp. 1014, with 358 illustrations. Baltimore: William Wood & Company, 1938.

THE 1938 YEAR BOOK OF RADIOLOGY. *Diagnosis:* Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital; Associate Editor: Whitmer B. Firor, M.D., Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. *Therapeutics:* Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York; Clinical Professor of Surgery, New York University Medical College, etc. Cloth. Price, $4.50. Pp. 512, with 511 illustrations. Chicago: The Year Book Publishers, Inc., 1938.

SURFACE AND RADIOLOGICAL ANATOMY FOR STUDENTS AND GENERAL PRACTITIONERS. By Arthur B. Appleton, M.A., M.D. (Cantab.), Professor of Anatomy in the University of London and Director of the Department of Anatomy in the Medical School of St. Thomas's Hospital, London, William J. Hamilton, M.D., B.Ch.(Belf.), D.Sc. (Glas.), F.R.S.E., Professor of Anatomy in the University of London at the Medical College of St. Bartholomew's Hospital, London, etc.,

and Ivan C. C. Tchaperoff, M.A., M.D., B.Ch. (Cantab.), D.M.R.E., Assistant Radiologist at St. Thomas's Hospital, London. Cloth. Price, $5.50. Pp. 311, with 338 illustrations. Baltimore: William Wood & Company, 1938.

Précis de technique radiographique. Par P. Porcher, radiologiste des Hôpitaux de Paris, avec la collaboration de A. Juquelier, assistant de radiologie des Hôpitaux de Paris. Cloth. Price, 150 fr. Pp. 332, with 302 illustrations. Paris: Gauthier-Villars, 1938.

Stratigrafia: metodo röntgenologico per la esplorazione analitica dei singoli strati sovrapposti. Alessandro Vallebona. Monograph in 2 volumes. Volume I, 100 pages; Volume II, 162 illustrations. Paper. Price, L. 50. Roma: Casa Editrice Luigi Pozzi, 1938.

A Handbook of Roentgen and Radium Therapy. By A. J. Delario, B.A., M.D., Radiologist, St. Joseph's Hospital, Paterson, N. J., and Community Hospital, Montclair, N.J. Cloth. Price $8.00. Pp. 362, with numerous engravings, graphs and tables. Philadelphia: F. A. Davis Company, 1938.

Meningiomas: Their Classification, Regional Behaviour, Life History, and Surgical End Results. By Harvey Cushing, M.D., Sometime Associate Professor of Surgery, Johns Hopkins University: Moseley Professor of Surgery, Harvard University, and Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston; Sterling Professor of Neurology, Yale University. With the collaboration of Louise Eisenhardt, M.D., Assistant Professor of Pathology, Yale University School of Medicine; formerly Associate in Surgery, Peter Bent Brigham Hospital, Boston. Cloth. Price, $15.00. Pp. 785, with 685 illustrations. Springfield, Illinois: Charles C. Thomas, 1938.

The Pituitary Gland: An Investigation of the Most Recent Advances. (Association for Research in Nervous and Mental Disease. Vol. XVII of a Series of Research Publications.) The Proceedings of the Association, New York, December 28th and 29th, 1936. Editorial Board: Walter Timme, Angus M. Frantz, Clarence C. Hare. Cloth. Price, $10.00. Pp. 764, with 160 illustrations. Baltimore: The Williams & Wilkins Company, 1938.

Röntgenatlas der Asbestose der Lungen. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, Ergänzungsband 54.) Von Prof. Dr. Erich Saupe, Röntgen- und Radium-Abteilung des Rudolf-Hess-Krankenhauses, Dresden. Paper, RM. 19.50; bound, RM. 21.50. Pp. 99, with 44 illustrations. Leipzig: Georg Thieme, 1938.

Der Kreuzschmerz in seiner Beziehung zur Wirbelsäule. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, Ergänzungsband 55.) Von Priv.-Doz. Dr. J. E. W. Brocher, Genf. Mit einem Vorwort von Prof. Dr. Volhard, Frankfurt a. M. Paper, RM. 19.50; bound, RM. 21.50. Pp. 91, with 101 illustrations. Leipzig: Georg Thieme, 1938.

Röntgendiagnostik der Gelenke mittels Doppelkontrastmethode. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, Ergänzungsband 56.) Von Dr. J. Oberholzer, Chefarzt am kantonalen Krankenhaus Wallenstadt, früher Oberarzt der chirurgischen Abteilung Kantonsspital Aarau/Schweiz. Mit Vorwort von Dr. Med. E. Bircher, A. Spitaldirektor Aarau. Paper, RM. 23.-; bound, RM. 25.- Pp. 128, with 134 illustrations. Leipzig: Georg Thieme, 1938.

Laboratory and Clinical Studies. Vol. XVIII. From the Memorial Hospital, Huntington Fund for Cancer Research, Douglas Research Laboratory. New York City, 1937.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

GOLDBERG, SAMUEL, and CANDIDO, JOSEPH L. Renal rickets. *Arch. Pediat.*, May, 1937, *54*, 291–299.

The authors briefly review the literature and present a case of renal rickets in a boy, aged six. Retardation of growth and development was first noticed at five months of age. Although the patient received adequate amounts of antirachitic vitimin D, he developed skeletal deformities, because of a probable early and persistent renal infection and insufficiency. The bony deformities grossly resembled those of juvenile rickets. Genu valgum was the most outstanding bony manifestation. Chemical studies of the blood revealed an increased nitrogen concentration with impaired renal function, although no disturbed relation between calcium and phosphorus could be demonstrated. The cause of the renal impairment was a bilateral pyohydronephrosis with hydroureters, which were noted clinically and confirmed at autopsy. Roentgen studies of the bones revealed changes more or less characteristic of juvenile rickets and consisted of diminished lime salts, trabeculation, osteoporosis and patchy ossification. Treatment along antirachitic lines was of no value and at times seemed definitely harmful.—*R. S. Bromer.*

WOLFF, WILLIAM A., and KERR, ELIZABETH G. The composition of human bone in chronic fluoride poisoning. *Am. J. M. Sc.*, April, 1938, *195*, 493–497.

Reports of chronic fluoride poisoning are rare though such poisoning has been attributed to excessive fluoride content in certain beers, and it has been known that significant percentages of it in the drinking water may produce mottling on enamel or noticeable chronic endemic

dental fluorosis. This type of poisoning has also been attributed to prolonged breathing of cryolite dust.

The author has studied biochemically various bones of the case which was reported by Bishop *et al.* The patient was a male negro, aged forty-eight, who had been exposed to finely ground rock phosphate dust almost daily for a period of eighteen years. This rock was found to contain 3.88 per cent fluorine. Roentgenologically, the following criteria were noted: intense coarsening of the trabeculations and density of the cortices; thickening of the pelvic girdle; roughening of the centra and calcifications in the attachments of ligaments. When dissected, the bones appeared thicker and their surfaces were rougher than normal, showing nodular or plate-like exostoses or "osteophytes." In cross section, the fluoride rib showed an abnormally thick cortex and very prominent trabeculae. The teeth were very brittle. Chemical analyses showed normal percentages of calcium, phosphorus and carbon dioxide but the fluoride content was increased up to 20-fold the normal. The highest concentrations of it were found in "softer bones," such as the sternum, ribs and vertebral column; the lowest percentages in the long bones. Since the carbon dioxide content remained normal, it seemed likely that the fluorine was deposited as a calcium or magnesium fluoride. The density of the bones appeared increased but actually their specific gravity was decreased. The fluoride bone was therefore more brittle.—*A. A. de Lorimier.*

Doub, Howard P. The roentgen aspect of sympathetic neuroblastoma. *J. Am. M. Ass.*, Oct. 9, 1937, *109*, 1188–1191.

Sympathetic neuroblastomas were first described by Marchand in 1891. Wright, in 1910, established them as a separate and distinct clinical entity. They are neurogenic in origin. Two disease syndromes have been described—the first, by Pepper, emphasizing the adrenal origin with early metastases in the liver, and the early age at which the tumor appears; the second, by Hutchinson, occurring somewhat later, and marked by metastatic lesions in the skull, orbits and long bones. Later studies have shown that these two types are indistinguishable pathologically and roentgenologically. They are seen most commonly in children under the age of four years. They are in all probability congenital.

The initial symptom in the author's 3 cases was pain referred to the spine and the legs. Frequent findings are an abdominal mass appearing early, loss of weight, swelling about the face or skull, proptosis of one or both eyes with discoloration of the lids, choked disc and enlarged glands. Usually there is a rapid decline followed by death in a few months. There may be manifestations of temporary improvement following radiation therapy, but relapse soon occurs. The most constant roentgenographic changes are those associated with bone metastases. The changes in the skull consist of widening of the sutures and increased digital markings, and of minute foci of absorption, producing a finely granular type of osteoporosis. The flat bones of the pelvis show a type of infiltration similar to that seen in the skull. In the long bones one may see elevation of the periosteum; areas of metastatic involvement, with bone resorption, more commonly in the ends of the diaphyses adjacent to the epiphyseal lines; and in many instances resorption of uneven density in these sites, suggesting a diffuse infiltration rather than a massive destruction, such as is seen in certain cases of osteoclastic carcinoma. Askin and Geschickter described these metaphyseal lesions as wedge shaped. The author has been impressed by the osteoporosis of an extreme grade involving the metaphyses in certain cases before actual dissolution of the bone structure takes place.

In cases in which a tumor mass is removed from the abdomen, the mass is usually seen to be solid and encapsulated. Askin and Geschickter found that metastasis to the retroperitoneal lymph nodes was more common than metastasis to the bones or liver. Histologically, these tumors are quite cellular and are composed of small cells with hyperchromatic nuclei and a narrow rim of cytoplasm. The author found that the tumors were moderately radiosensitive. The clinical course was rapidly downward, with only temporary remission after radiotherapy. The average length of life from the time of the first observation of the patient until death was four and one-third months.—*S. G. Henderson.*

Barr, J. S., Hampton, A. O., and Mixter, W. J. Pain low in the back and "sciatica" due to lesions of the intervertebral disks. *J. Am. M. Ass.*, Oct, 1937, *109*, 1265–1270.

In previously published papers attention was

drawn to the rôle of the intervertebral discs in causing intractable "sciatic" radiation of pain from pressure of herniated disc tissue on one or more roots of the cauda equina in the lower lumbar region. The diagnosis of rupture of an intervertebral disc should be considered in the study of every case of strain low in the back and "sciatica." This paper deals with a study of 58 patients with proved rupture of an intervertebral disc in the lumbar region. In case of rupture of a lumbar intervertebral disc with pressure on one or more roots of the cauda equina, the patient is usually a healthy, vigorous man whose chief complaint is pain radiating unilaterally down the posterior part of the thigh and the posterolateral part of the calf. There may be numbness or tingling in the involved extremity, bilateral radiation of pain, muscular weakness or paralysis and incontinence of urine or feces. A history of trauma to the lower part of the back was obtained in about 80 per cent of the authors' cases. The most common type of trauma was sustained when the patient was lifting a heavy weight and felt something "give way" in the lower part of the back. On physical examination, limitation of motion of the lumbar part of the spine by muscle spasm is the most characteristic observation. The usual lumbar lordosis is diminished. Kyphosis may be present. A fixed list ("sciatic scoliosis") of the lumbar part of the spine is commonly noted. Straight leg raising is limited. Neurologic changes may be totally absent. The most common neurologic finding is absence or diminishing of the ankle jerk on the affected side.

If the history, physical examination and ordinary roentgenograms suggest the possibility of a ruptured disc, lumbar puncture is indicated. It should be done as low as possible, preferably at the lumbosacral articulation, and 2 to 5 cc. of fluid should be removed, and examined for total protein content. Elevation of the total protein content is apparently due in most instances to irritation of the nerve roots. Elevation of the total protein above 40 mg. per 100 cc. was present in all but 6 of the authors' cases. If the content is elevated, one should proceed with the diagnostic use of iodized oil. Regular roentgenograms of the lumbar part of the spine cannot be relied on as an indication for or against the injection of iodized oil. Sciatic scoliosis and partial obliteration of the normal anterior lordotic curve of the lumbar part of the spine occurred in most of the cases. Schmorl's nodule in the body of a vertebra was seen only occasionally and is purely an incidental observation.

The roentgenoscopic examination after the injection of iodized oil is the most important step in the diagnosis. Five cubic centimeters of iodized poppy-seed oil is injected into the lumbar canal. The advantage of films taken during roentgenoscopy cannot be overestimated. The patient is manipulated by tilting the table under roentgenoscopic control. Since the lesion to be demonstrated is a small, anteriorly placed extradural nodule at the disc levels, the iodized oil must be brought into contact with the anterior dural surfaces, and in order to do this the patient must lie face down on the table. A constant filling defect in any region is recorded by serial roentgenograms taken in various angles of rotation of the patient.

The posterior rupture of the intervertebral disc which produces unilateral symptoms consists of a rounded nodule 1 cm. or more in diameter. This nodule lies just lateral to the strong central portion of the posterior longitudinal ligament and is directed toward the lamina of the vertebra. It is the purpose of the roentgen examination to demonstrate filling defects corresponding to this rounded mass and the displaced nerve roots. Asymmetrical filling of the nerve sheaths is a normal observation. If no filling defect is seen in the anteroposterior view the examination is considered to show no evidence of ruptured disc. The lateral view is seldom of definite value because the defect is unilateral and is not usually seen in this view, being obscured by dense iodized oil which occupies the normal side of the canal. The fifth disc area can usually be more accurately examined several days after the oil been injected, because more complete filling of the nerve sheaths and lateral portion of the canal will take place. For this reason the authors usually re-examine within one or two weeks all patients whose examinations gave negative results.

The filling defect of the ruptured disc fragment was demonstrated in each of a consecutive series of 31 patients examined with iodized oil. Microscopic examination of the removed specimen reveals that it is identical with the normal intervertebral disc. Sometimes it is from the annulus fibrosus and sometimes from the nucleus pulposus; often elements of both tissues are present.

Almost every patient is immediately relieved

of pain in the leg after operative removal of the ruptured disc. Eight cases in this series were operated upon too recently to be included in the study of the end results. Of the remaining 50 patients, 32 recovered completely. Twelve additional patients were markedly improved, but complained of slight residual pain or weakness in the back. Two patients had relapses and there was 1 postoperative death.

Prolonged, adequate, conservative orthopedic care should be insisted on in every case of suspected rupture of an intervertebral disc before iodized oil is used.—*S. G. Henderson.*

Weil, M. P., and Lalanne, L. Contribution à l'étude des ligamentites vertébrales; du rôle du ligament dans la production des ostéophytes. (A contribution to the study of the vertebral ligaments; the rôle of the ligament in the production of osteophytes.) *Presse méd.*, Jan. 22, 1938, *46*, 123–125.

There are two types of new bone formation in the spine: (1) The osteophyte which is characteristic of degenerative osteoarthritis. This is new bone with a smooth outline, and a cortex arising from the vertebral body and continuous with it, where the cartilaginous covering ends. (2) The syndesmophyte, characteristic of rhizomelic spondylosis of Pierre Marie, which is a simple ligamentary calcification without cortex and structure, following the outline of the ligament, extending longitudinally along the vertebral column but not widening the bodies nor bridging them laterally.

Although, after a certain stage of development, these processes appear different, roentgenologically the difference does not seem fundamental. Both processes, at the onset, extend in the direction of the ligament whose shape they will assume. Although characteristically rhizomelic spondylosis gives rise to regular new bone formation it may be formed irregularly. Besides there are mixed types which are believed to be degenerative states in which ligamentous calcifications are added to osteoarthritis.

Anatomical study was made of 10 cases: 4 of spondylosis, 6 of osteoarthritis, which showed the following: The lesions of rhizomelic spondylosis are characterized ordinarily by a smooth and regular bony path which follows the vertebral ligaments perfectly. This is pathognomonic but is not constant nor exclusive. On the other hand, degenerative vertebral osteoarthritis often gives rise to osteophytes which follow the shape of the ligaments.

Coexistence of osteophytes and syndesmophytes is therefore commonplace. Whichever the primary disease, the new formation, shown roentgenographically, follows the direction of the ligament. Later, and at a distance from their origin, the new formations assume new orientations, deviate and bridge vertebrae. They may or may not remain stationary. They may remain smooth or become irregular, depending perhaps on conditions of development of the lesion, the rapidity of development and the importance of the displaced calcific material. In no case is there true new bone formation: the bone formation in the osteophyte is not normal bone. Hence, the isolated lesion does not permit of a differential diagnosis; only when examined in the light of other lesions investigated roentgenologically, can a diagnosis be made.—*M. L. Sussman.*

Mezzari, A. Über die Calvésche Vertebra plana (infantile Pseudospondylitis). (Calvé's vertebra plana (infantile pseudospondylitis).) *Fortschr. a. d. Geb. d. Rontgenstrahlen*, March, 1938, *57*, 275–286.

Under the title "A localized affection of the spine, suggesting osteochondritis of the vertebral body with the clinical aspects of Pott's disease," Jacques Calvé described a new disease syndrome. Since 1924, 27 cases have appeared in the literature, but in only 17 is the diagnosis entirely acceptable. The symptoms are pain radiating from the spine, lack of desire to play, ease of fatigue particularly in the upright position and when walking. The signs are point tenderness to pressure over the spine accompanied by rigidity and slowly developing angular kyphosis. No abscesses or fistulas develop as in tuberculous spondylitis. The roentgen appearance is very characteristic. The disease occurs from two to fifteen years of age, but is most common from four to seven, with rapid onset over a period of months and then slow healing over a period of years. The author's patient was a syphilitic child of seven years and both of the parents were also syphilitic. Some antiluetic treatment was given immediately after birth. There had been pain in the dorsolumbar region for six months before the roentgen examination which showed marked flattening of the twelfth dorsal body. During a year of hos-

pital treatment the body showed evidence of regeneration. Then death occurred after a three day course of tracheobronchial diphtheria, and an autopsy was obtained. Pathological studies showed the narrow vertebral body but otherwise the spongy network and the process of growth appeared fairly normal. The author speculates as to the pathogenesis of the disease and regards it as an aseptic necrosis in this instance due to syphilitic affection of the vasomotor nerves controlling the circulation in this body. The disease does not belong to the congenital rachitic deformities as suggested by Zanoli.—*W. A. Evans, Jr.*

BRAILSFORD, JAMES F. Radiographic detection of myelocele of the unborn foetus. *Lancet*, May 14, 1938, *1*, 1106–1107.

Myelocele results from incomplete fusion of the neural folds. It is incompatible with life. Just as in cases of monsters, anencephaly, hydrocephaly and severe spinal deformities, roentgenology offers the sole means of its prenatal recognition.

Normally, prenatal roentgenography reveals a uniform kyphosis in the spine of the fetus. This involves the cervical, dorsal and lumbar portions but does not include the sacral, the latter appearing flattened out, being directed slightly posteriorly. From the cervical to the lumbar regions the vertebral bodies show a gradual increase in size. The middle thoracic and upper lumbar vertebrae are the latest to ossify and may appear "bobbin-shaped," because of notching in the anterior and posterior aspects where ossification has not taken place. The length of the pedicles appears about equal to the anteroposterior dimension of the bodies and, when the articular processes are also visualized, the dimensions of the vertebrae appear to be about twice that of the bodies. In anteroposterior projection, the bodies may show a notching in both the superior and inferior surfaces and in addition two small channels of increased roentgenographic density—due to venous channels.

The roentgen criteria in cases of myelocele include: (1) a conspicuous "hump" usually including about 6 vertebrae, superimposed upon the normal kyphosis; (2) little or no development of laminae or processes on the vertebrae of the "hump"; (3) lateral deviation in the position of the laminae and processes of those vertebrae near to the more involved segments of the "hump" (as visualized by the anteroposterior projection); (4) reduction in the total length of the spine; (5) possibly, lack of fusion of the two nuclei concerned with bodies of the vertebrae in the "hump"; (6) in severe cases, possibly, defects throughout the entire length of the spine associated with anencephaly or hydrocephalus.—*A. A. de Lorimier.*

BLOOD AND LYMPH SYSTEM

BARTSCH, JULIAN. Röntgendiagnostik der Gallenblase bei Anämie (Anaemia perniciosa). (Cholecystographic findings in anemia (pernicious anemia).) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1938, *57*, 295–298.

In 29 of 32 cases of pernicious anemia there was failure of the gallbladder to become visualized after oral administration of the gallbladder dye. Subsequent studies after a rise in the red cell count showed visualization. Two of the 3 other cases had gallstones.—*W. A. Evans, Jr.*

GENERAL

FRIEDRICH, H., and VEIEL, E. Röntgendiagnose des Echinococcus alveolaris. (Roentgen diagnosis of echinococcus alveolaris.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, April, 1938, *57*, 366–374.

This disease is very rare, never occurring in north Germany and only rarely in the south. Some places like Tübingen and Memmingen have a higher incidence and appear to be sources of infection. Echinococcus disease occurs in two forms, the one with thin walled sacs filled with the small echinococcus vesicles, the other consisting of firm, hard, infiltrating growing tissue. This latter or alveolar form has many characteristics of malignant tumor tissue, occurs predominantly in the liver, and on palpation is commonly mistaken for liver carcinoma. Rarely the lungs are involved, and more rarely the brain, soft parts, or skeleton. The author has had no personal experience in the use of skin tests, but says it is difficult to obtain potent antigen because of the rarity of the disease. The complement fixation reaction was positive in only one-half of his cases. A pronounced eosinophilia was found in only one case. The patients show many manifestations which would point to gastric or intestinal carcinoma, that is epigastric pressure, gradually increasing weakness, emaciation, and a pale yellow skin. The palpation of a nodular hepatic

tumor makes one think of carcinomatous metastasis, but when the gastrointestinal tract shows no evidence of primary lesion, one should next think of the infiltrating type of echinococcus infection. This diagnosis is the more likely when the condition has been present for a long time without much change.

The roentgen examination of the upper abdomen will often make the diagnosis conclusive. This is based on the peculiar calcium deposits which occur in the tissue masses of the liver. The author has not seen calcium deposits in other types of liver tumor. In only one of the author's cases was it not possible to demonstrate the calcification in the echinococcus tissue of a large liver mass. Illustrations are included showing the roentgen appearance in the author's 5 cases.—*W. A. Evans, Jr.*

ROENTGEN AND RADIUM THERAPY

Meyer, A. Indications, techniques et résultats de la radiothérapie des états inflammatoires des amygdales et du rhino-pharynx. (Indications, technique and results in radiotherapy of inflammatory states of the tonsil and nasopharynx.) *Bull. et mém. Soc. d'électro-radiol. méd. de France*, Jan., 1938, *26*, 48–52.

This form of therapy was based upon: (1) the action of roentgen rays in producing a regression and even destruction of lymphoid disease; (2) the favorable effect on inflammation. The author's factors were 200 kv. 1.0 to 1.5 mm. copper plus 2.0 mm. aluminum; distance 30 cm.; field, 4.8 cm. diameter.

The small field limits irradiation of the healthy glands of the neck. The two sides are irradiated alternately, 200 to 400 r being given at each sitting; two to three treatments are given per week. In the chronic cases, up to a total of 2,000 to 4,000 r (i.e., 1,000 to 2,000 r per field) was applied.

Usually there is a slow regression of the tonsil without any troublesome reaction in the mucous membrane of the skin. The crypts enlarge and the inflammation subsides. Of the 27 cases treated, 18 cases could be followed; 14 were completely cured, 4 ameliorated.

Summary: (1) In acute inflammation (acute angina) very small doses (50 to 100 r) are used. (2) Chronic tonsillitis, repeated angina, chronic angina with renal, joint and venous metastasis; a total dose of around 2,500 r. (3) Carriers of streptococcus and diphtheria; 500 to 1,000 r. (4) Certain foci of tonsillar hypertrophy where surgical removal is contraindicated or in cases where repeated difficult surgery is necessary, 1,000 to 4,000 r, depending on the state of sclerosis. Simple hypertrophied tonsils should be removed surgically.—*M. L. Sussman.*

Carty, John R., and Rude, Joe C. Some notes on the x-ray treatment of enlarged inflammatory tracheobronchial lymph nodes in infants and children. *Arch. Pediat.*, Jan., 1937, *54*, 26–29.

The authors consider roentgen therapy of infected lymphadenopathy of the tracheobronchial glands in infants and children a valuable form of treatment. The history and symptomatology are very important and must be carefully considered if there is to be a proper selection of cases. There is often a history of whooping cough, measles or scarlet fever; a history of frequent colds or sore throats is very common; at times a previous acute or chronic sinusitis is found; less frequently, there is a history of middle ear disease.

There are four important symptoms: cough, low-grade fever, slight pallor, and finally, failure to gain. The cough has a peculiar, annoying, insistent, irritating quality; it is usually dry, sometimes brassy, and not infrequently is aggravated at night, and may even be paroxysmal, especially if there has been a previous attack of pertussis. It may last for months. A slight pallor and anemia are common with failure to gain in weight and with general listlessness.

As a part of the clinical examination, the usual routine for the exclusion of tuberculosis should be followed. Calcification within the tracheobronchial lymph nodes and a positive tuberculin reaction even in higher dilutions are not contraindications for therapy, provided the history and symptomatology indicate an infectious element. Careful roentgenoscopic and roentgenographic examinations should always be made of the chest before starting treatment. The former is done in the various positions. Posteroanterior and oblique roentgenograms are then made. The diaphragm shadows may be lower than usual, and the lung fields show a hyperventilation at times. There is an increase in linear vascular markings. The hilar shadows may be enlarged and lobulated or merely denser than normal. There may be a widening of the supracardiac shadow with or without lobulated borders. Sometimes the only abnormal findings

noted may be a clouding of the mid-third of the posterior mediastinal space, seen only during roentgenoscopy in the right anterior oblique position.

If during the general examination, an infected focus is found, such as the tonsils, sinuses etc., everything should be done to clear up these conditions. This may be done during the course of the roentgen treatment or as soon after the completion of the treatment as is convenient. Following therapy, there is usually exacerbation of the symptoms, particularly the cough. The cough then gradually disappears and the patient gains in weight. A check roentgen examination is made of the chest three to four weeks following the last treatment. There is usually a decrease in size of the supracardiac shadow and an increase in sharpness of outline.

The factors of technique are as follows: 200 kv. (peak); distance of target from skin, 50 cm.; filtration, 1 mm. of copper and 3 mm. of aluminum; 50 to 100 r, measured in air, at each treatment. Four treatments will usually suffice but in older children it may be necessary to give six. They are given at weekly intervals through two portals to the mediastinum, one in front and one in back, per treatment.—*R. S. Bromer.*

ERF, LOWELL A., and FINE, ARCHIE. Serial blood and bone marrow findings of an eight-month premature and its roentgen ray treated chronic, myeloid leukemic mother. *Am. J. M. Sc.*, Jan., 1938, *195*, 8–17.

The authors were able to find, reported in the literature, only 30 cases where pregnancy was complicated by leukemia.

They report a case of a woman who was first studied in September, 1935, at which time she had lost weight from 205 to 165 pounds. She complained of a dragging sensation in her left upper quadrant, early sensation of fullness after eating, tendency toward ecchymoses, recent development of menorrhagia and dysmenorrhea. She had had 5 children during the previous twelve years, all living and well. Her white cell count was 310,000 while the red cells were down to 2,750,000. Physical and roentgen studies revealed a very large spleen. She was given a course of roentgen therapy (dosages not stated) with complete reduction of the spleen. Then 560 r (120 kv.,5 ma., 3 mm. Al) was applied to the hypogastric region, with the intent of sterilization. In August, 1936, recurrence of the leukemia was evident and 1,800 r was given to the spine and splenic regions. By December another exacerbation developed and another treatment of 1,800 r was given. It was then realized that the patient was carrying about a six-month pregnancy. Abortion was recommended but the surgical procedure was not accomplished until February, 1937, when a 5 lb. 13 oz. premature male infant was delivered. Complete blood counts were made of the mother's blood, the cord blood and the infant's blood, and serially, sternal punctures were studied, in the case of the mother, and sternal and tibial smears, in the case of the infant. The mother showed a slight increase in leukemic activity, after delivery. This episode was controlled by roentgen therapy, but exacerbations recurred at intervals; these were treated with dosages of 200 to 300 r per field, treatments being given at intervals of three to four days through portals of 10 or 15×20 cm., these extending from the cervical to the sacral spine and including the splenic areas. Reactions of white cell counts as low as 5,000 prompted transfusions. The patient died about seven months after her delivery.

All blood counts and smears made by puncture of the sternum and tibia, in the case of the infant, were normal. The authors emphasize the fact that there has been no authentic case of leukemia in the offspring of leukemic mothers, though there have been definite examples of leukemia in infancy, the offspring of normal parents.—*A. A. de Lorimier.*